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IMPLANTATION OF HOLLOW GROOVED BODY INTO ORBIT FOR FILLING

LATE AFTER ENUCLEATION OF EYEBALL

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NEW YORK

Many authors have described or advocated implantation of various substances into Tenon's capsule immediately after removal of the eyeball. This paper is not concerned with these procedures but rather with the introduction of a body behind Tenon's capsule late after healing from enucleation has taken place. A sharp distinction should be made between putting filling into Tenon's capsule while it is open and putting filling behind the organized mat of Tenon's capsule that results from collapse of the walls of the cavity and healing of the flaps of the capsule that come in apposition behind the conjunctival covering of the fundus of the socket.

Patients object to an appearance of sinking of an artificial eye and particularly to sinking below the upper orbital margin above the artificial eye. Along with the sinking there is, in some degree, smoothing of the fold of the upper lid. For such a deformity implantation should not be made into the upper part of the orbit but into the muscle cone behind the fundus of the socket. This tends to correct the backward position of the prothesis and to carry to their proper place the structures that belong in the upper part of the orbit. Such an operation is particularly indicated in cases of traumatic injury with defects in the floor of the orbit, with letting down and loss of orbital contents. In some cases filling along the floor as well as in the muscle cone may be needed. For implantation along the floor, fascia lata is used. For filling inside the muscle cone, different substances have been used, among them vital tissues, such as fascia, cartilage, bone and fat. There seems to be no advantage in the use of vital tissue, as a properly placed nonvital body can stay in place indefinitely and hold its own against contraction. If the contents of the orbit are not badly injured, fat may

† Dr. Wheeler died Aug. 22, 1938.

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be satisfactory, but if there is considerable scar tissue in the orbit, a fat graft is liable to contract. Moreover, in several cases proliferation has taken place in a fat graft, with the formation of lipoma.

Smooth spheres of gold or glass have been used, and they could be recommended except that after a period of weeks, months or years they are liable to migrate from the muscle cone, taking with them their capsules of newly formed tissue with which they have become surrounded. Some years ago, conscious of the frequent misbehavior of smooth spheres in the muscle cone, I implanted cork. The implant was cut in the form of a sphere, and then four grooves were cut in the sphere, each groove to receive one of the four rectus muscles. These grooved spheres stayed in place well, but a peculiar phenomenon made their use inadvisable. Long after their implantation the tissues in front of them sloughed, and they appeared in the cul-de-sac. Why this happened I do not know, but I suppose that some chemical change took place with a degree of disintegration of the cork and necrosis of the tissue about the cork. The success that I met with, as far as the staying in place of the grooved spheres of cork was concerned, led me to the use of a smooth body made of glass. A glass blower made the four grooves to receive the four rectus muscles, and implantation of this body has been rewarded by permanent good results. Roentgenograms have demonstrated that the axis of the grooved sphere corresponds with the axis of the orbit, so probably the rectus muscles stay permanently in the grooves. So far, none of these bodies has given trouble late after implantation. Figure 1 shows the smooth glass body with the four grooves made to receive the rectus muscles.

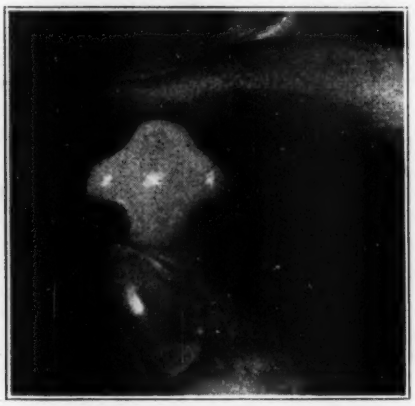

Fig. 1.—Hollow glass body for implantation behind Tenon's capsule late after enucleation of the eyeball. Notice the four grooves for the reception of the four rectus muscles.

OPERATIVE TECHNIC

Block anesthesia of the orbit is not fully effective. Infiltration of the orbit with procaine hydrochloride is permissible, although it entails the disadvantage of partially filling the orbit which is to receive the sphere and so putting Tenon's capsule on the stretch at the conclusion of the operation. Avertin or avertin and ether inhalation are satisfactory.

An ordinary speculum is introduced to expose the fundus of the socket. With a knife or scissors, a horizontal incision is made through the conjunctiva completely across the fundus behind the palpebral fissure (fig. 2 *A*). The conjunctiva is dissected from Tenon's capsule freely with scissors and with the least possible

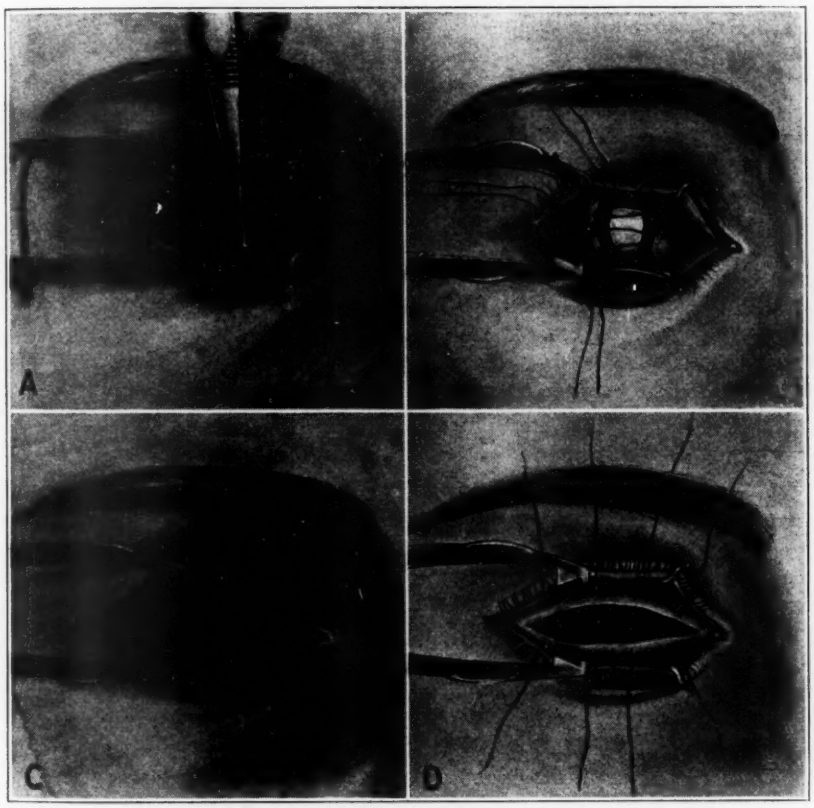

Fig. 2.—Steps in the operative procedure. In *A*, with the speculum in place, a horizontal incision is made in the conjunctiva completely across the fundus of the socket. In *B* the conjunctiva has been dissected from the underlying Tenon's capsule, and the conjunctival flaps have been placed in the blades of the speculum with the eyelids. A vertical incision has been made through Tenon's capsule deep into the orbital tissue. A hollow grooved body has been placed in the orbit, and sutures have been placed to cause overlapping of the flaps of Tenon's capsule. In *C* the overlapping flaps of the capsule are secured by 000 chromic catgut sutures. In *D* the conjunctiva is released from the blades of the speculum and the conjunctiva is closed by fine silk or catgut sutures.

traumatism. Then the conjunctiva is taken in the blades of the speculum along with the lids. A vertical incision is made in Tenon's capsule, and the dissection is carried into the orbital tissue within the muscle cone. As the orbital dissection is carried backward, it should take the direction of the axis of the orbit and pass nasalward toward the apex; otherwise the external rectus muscle is liable to be cut. The orbital incision should go to within about 1 cm. of the orbital apex. Usually the ophthalmic artery need not be cut, but occasionally it is injured, and it may have to be clamped. The mat of Tenon's capsule is dissected up a few millimeters on each side of the vertical incision. If the orbital dissection is adequate, the grooved sphere will slip easily into the newly formed cavity within the muscle cone. The direction of the grooves in the implant and their position should be such that the four rectus muscles will fit into them. The axis of the implant then corresponds approximately with that of the orbit. It should be pressed well back into the orbit. Mattress sutures of fine chromic catgut are placed in Tenon's capsule, so that there will be an overlapping of the flaps of the capsule of 4 or 5 mm. Figures 2 *B* and *C* illustrate the manner in which the flaps are brought squarely into an overlapping position. For this suturing, atraumatic needles are of advantage, as the needles and suture material slip through almost without resistance. Next, the conjunctival flaps are raised from the blades of the speculum, and the horizontal conjunctival wound is closed by fine silk or catgut sutures, as shown in figure 2 *D*. A firm pressure dressing should be applied at the conclusion of the operation and left in place for about one week. The pressure will hold the flaps accurately in place and will prevent hemorrhage into the orbit. The conjunctival sutures may be removed when the pressure dressing is taken off, and a light dressing may be worn for a few days. The socket is ready for a prosthesis three weeks after operation.

DISCUSSION

Dr. Clyde E. McDannald: What is the approximate size of these implants, and what are the possibilities of erosion of a glass implant? I bring up this question of erosion because when I was an intern at the New York Eye and Ear Infirmary a man appeared one day with severe pain in his eye and stated that he had undergone a Mule's operation thirteen years previously in London. He had taken out his handkerchief, and wiped his eye, and since then he had had severe pain. I referred him to one of the surgeons, who found that the ball had completely eroded and broken into innumerable fine particles. I wonder if there is a possibility of this taking place with the implant described here.

Dr. John M. Wheeler: I do not know. I have been doing the operation that I am advocating for a little over three years, and that is too short a time to judge on the particular point of possible erosion. I remember the case Dr. McDannald spoke about; it is the only one of its kind of which I have heard. The implantation was made into the sclera, but implantations of glass by the hundreds were done on American soldiers during the World War. As far as I know none of the implants has disintegrated. I think that glass or gold placed in the orbit behind Tenon's capsule will stay indefinitely. At least, I hope so.

The grooved glass implants have been made by Mager and Gougelman in different sizes, but I think that the implant of preference is one with an anteroposterior diameter of 18 mm.

DETERMINATION AND SIGNIFICANCE OF THE SCOTOPIC RETINAL VISIBILITY CURVE

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For the past half century the relation between visual purple and vision has been realized to be of fundamental importance. Many investigators [1] have compared the absorption spectrum of visual purple with the scotopic visibility curve. Some of the more recent comparisons have been made by Hecht and Williams,[2] Dartnall and Goodeve [3] and Blum.[4] The comparisons made by Hecht and Williams and by Blum are inadequate because the absorption spectrum of visual purple was compared with the scotopic ocular visibility curve, which means that no corrections were made for the selective absorption of light by the refractive media of the human eye. These comparisons are also inadequate because the absorption spectrum of visual purple used was that determined by Koettgen and Abelsdorff,[1c] whereas the more recent work of Lythgoe,[5] of Krause and Sidwell [6] and of Bayliss, Lythgoe and Tansley [7] has shown that the absorption of light of short wavelengths by visual purple is much greater than was formerly supposed.

From the Howe Laboratory of Ophthalmology, Harvard University, and the Massachusetts Eye and Ear Infirmary.

1. (*a*) Trendelenburg, W.: Quantitative Untersuchungen über die Bleichung des Sehpurpurs in monochromatischem Licht, Ztschr. f. Psychol. u. Physiol. d. Sinnesorg. **37**:1, 1905. (*b*) Koenig, A.: Ueber den menschlichen Sehpurpur und seine Bedeutung für das Sehen, Sitzungsb. d. k. Akad. d. Wissensch., 1894, p. 577. (*c*) Koettgen, E., and Abelsdorff, G.: Absorption und Zersetzung des Sehpurpurs bei den Wirbeltieren, Ztschr. f. Psychol. u. Physiol. d. Sinnesorg. **12**:161, 1896. (*d*) Hecht, S.: The Visibility of the Spectrum, J. Optic. Soc. America **9**:211, 1924. (*e*) Venable, W. M.: The Absorption Spectrum of Visual Purple, ibid. **10**: 133, 1925.

2. Hecht, S., and Williams, R. E.: The Visibility of Monochromatic Radiation and the Absorption Spectrum of Visual Purple, J. Gen. Physiol. **5**:1, 1922.

3. Dartnall, H. J. A., and Goodeve, C. F.: Scotopic Luminosity Curve and the Absorption Spectrum of Visual Purple, Nature, London **139**:409, 1937.

4. Blum, H. F.: Visual Purple and Rod Vision, Science **87**:193, 1938.

5. Lythgoe, R. J.: The Absorption Spectra of Visual Purple and of Indicator Yellow, J. Physiol. **89**:331, 1937.

6. Krause, A. C., and Sidwell, A. E.: The Absorption Spectra of Visual Purple and Its Photodecomposition Products, Am. J. Physiol. **121**:215, 1938.

7. Bayliss, L. E.; Lythgoe, R. J., and Tansley, K.: Some New Forms of Visual Purple Found in Sea Fishes, with a Note on the Visual Cells of Origin, Proc. Roy. Soc., London, s.B **120**:95, 1936.

The comparison made by Dartnall and Goodeve,[3] although they used modern data on the absorption spectrum of visual purple, is inadequate because again the comparison was made with the scotopic ocular visibility curve. It is essential that the modern data on the absorption spectrum of visual purple be compared with those on the scotopic retinal visibility curve. In order to determine the scotopic retinal visibility curve, it is necessary to transform the scotopic ocular visibility curve by allowing for the selective absorption of light by the refractive media of the human eye. This transformation has hitherto been impossible because of lack of the necessary data. The only available quantitative data relating to this subject are those of Roggenbau and Wetthauer [8] on the bovine eye. Unfortunately, one cannot assume that the absorption spectrum of the bovine eye is the same as that of the human eye. Among many other differences, the bovine eye is larger and younger than the adult human eye. In fact, that the limits of transmission of the ocular media in the violet and ultraviolet portions of the spectrum vary considerably with the genus of animal has been shown by Shoji.[9] Recently, in collaboration with E. F. McCarthy, I determined the absorption spectrums of the refractive media of each of several optically normal human eyes. A description of the apparatus and of the method used in this investigation and also of the results has appeared in an article in the ARCHIVES.[10] The purpose of the present paper is to present a comparison between the absorption spectrum of rhodopsin and the scotopic retinal visibility curve and to discuss the significance of the agreement found.

The comparison made by Hecht and Williams [2] is shown in chart 1. The data of Koettgen and Abelsdorff[1c] at 420, 440, 640 and 660 millimicrons were discarded by Hecht and Williams on the grounds that they had been inadequately determined. The discrepancy between the positions of the two curves on the wavelength axis was explained by Hecht and Williams in terms of Kundt's rule, according to which the absorption spectrum of a substance in solution moves toward the long wave end of the spectrum as the refractive index of the solvent increases. They pointed out that the absorption spectrum of visual purple is obtained while the visual purple is in dilute bile salts solutions. They assumed that the visual purple in the living retina is in

8. Roggenbau, C., and Wetthauer, A.: (*a*) Zur Frage der Erwärmbarkeit der einzelnen lichtbrechenden Teile des Auges nach Bestrahlung durch einen leuchtenden Körper, Ztschr. f. Augenh. **64**:143, 1928; (*b*) Ueber die Durchlässigkeit der brechenden Augenmedien für langwelliges Licht nach Untersuchungen am Rindsauge, Klin. Monatsbl. f. Augenh. **79**:458, 1927.

9. Shoji, Y.: Untersuchung über die Absorption der ultravioletten Strahlen durch die Augenmedien, Mitt. a. d. med. Fakult. d. k. Univ. zu Tokyo **29**:61, 1922.

10. Ludvigh, E., and McCarthy, E. F.: Absorption of Visible Light by the Refractive Media of the Human Eye, Arch. Ophth. **20**:37 (July) 1938.

some sense in solution in the rods, saying that "The terminal segments of the rods are, from all observations and descriptions, fairly dense and highly refractive bodies. . . . It is in these that the visual purple is dissolved in the living retina." They suggested: "The difference in the positions of the two curves is explainable in terms of Kundt's rule. This would assume that the visual purple we can extract from the eye and whose maximum of absorption in bile salts solution is at 503 μμ, is present in solution in the rods where its absorption maximum is at 511 μμ, and in very dilute solution in the cones where its maximum is at 554 μμ (or more probably, as corrected for macular transmission, at 540 μμ)." This explanation of the difference between the two curves in chart 1 seems inadequate. It has been pointed out

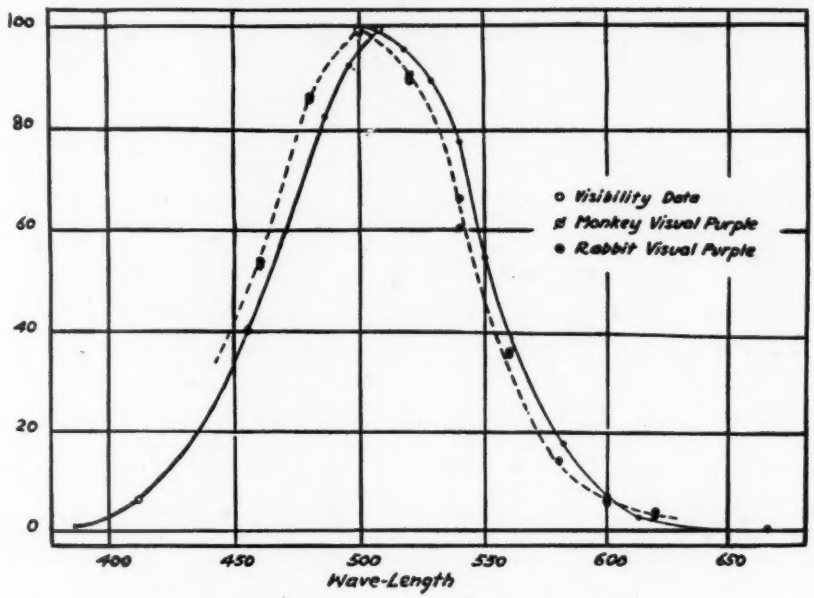

Chart 1.—The solid line is the scotopic ocular visibility curve in terms of energies (Hecht and Williams); the dash line, the absorption spectrum of visual purple (Koettgen and Abelsdorff).

by Dartnall and Goodeve [3] and also by Blum [4] that Kundt's rule is unreliable. Krause [11] has noted that according to Kuhne dried visual purple is fairly light-stable. This lends weight to his suggestion that the reaction of visual purple to light may involve water and be bimolecular, a bimolecular reaction occurring in a large excess of water, giving the appearance of a unimolecular reaction. Tansley [12] has

11. Krause, A. C.: The Biochemistry of the Eye, Baltimore, Johns Hopkins Press, 1934, p. 76.

12. Tansley, K.: The Regeneration of Visual Purple: Its Relation to Dark Adaptation and Night Blindness, J. Physiol. **71**:442, 1931.

pointed out that the results of her experiments on the amount of visual purple present in the retinas of dark-adapted rats may be expressed by the equation for a unimolecular reaction. This evidence and also the high water content of the retina suggest strongly that even though rhodopsin may be in the terminal segments of the rods, it may still be in weak aqueous solution. In this case Kundt's rule could not validly be used to explain the discrepancy between the two curves even if it were known to apply to solutions of visual purple.

As a matter of fact, however, Kundt's rule would have to accomplish a great deal more than correct the difference between the two curves in chart 1. In chart 2 the data of Hecht and Williams on the scotopic ocular visibility curve and the modern data of Lythgoe [5] on

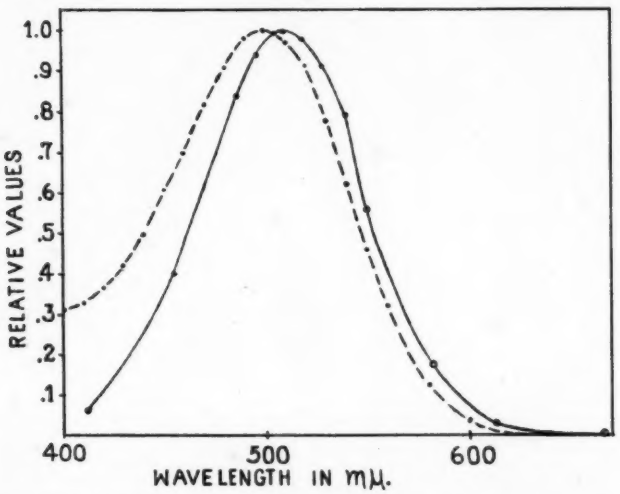

Chart 2.—The solid line is the scotopic ocular visibility curve in terms of energies (Hecht and Williams); the dash line, the absorption spectrum of visual purple (Lythgoe).

the absorption spectrum of visual purple are shown for comparison. Lythgoe's values for p_H 7.0 were used. According to Nakashima,[13] the p_H of the dark-adapted retina is about 7.3. Lythgoe's values for p_H 7.0 and p_H 7.6 are so nearly the same, however, that interpolation did not seem warranted. It may be noted in passing that the data of Krause and Sidwell [6] on bovine visual purple are in essential agreement with those of Lythgoe [5] on the visual purple of the frog. It is seen in chart 2 that not only is there a considerable discrepancy between the maxima of the two curves but the curve representing the absorption spectrum of rhodopsin is much higher in the blue end of the spectrum

13. Nakashima, M.: Beiträge zur Kenntnis des Sehpurpurs, abstracted, Zentralbl. f. d. ges. Ophth. **22**:772, 1930.

than that representing the scotopic ocular visibility curve. Even if Kundt's rule were operative and shifted the dash line curve about 9 millimicrons to the right so that the maxima of the two curves coincided, a great discrepancy in the blue end of the spectrum would still remain.

The reasoning which causes one to expect agreement between the absorption spectrum of rhodopsin and the scotopic retinal visibility curve is as follows: It is believed that visual purple is the light-sensitive substance involved in rod or scotopic vision. According to the law of photochemistry enunciated by von Grotthus [14] and Draper,[15] only that light which is absorbed can initiate a chemical change. Hence, if visual purple is the photosensitive substance for scotopic vision, the sensitivity of the rods to light of different wavelengths must be dependent on the extent to which light of various wavelengths is absorbed by rhodopsin. Furthermore, Einstein's [16] law of photochemical equivalence, or the law of Stark [17] and Einstein, states essentially that the number of molecules of the absorbing substance which decompose is equal to the number of quanta absorbed. The question as to whether or not this law may be applied to other than the first stage of the photochemical reaction need not be of concern here, particularly in view of the fact that Dartnall, Goodeve and Lythgoe [18] appear to have demonstrated that the quantum efficiency of the reaction is probably 1. The scotopic ocular visibility curve is determined by finding for different wavelengths the amount of energy to which the eye must be subjected in order to produce a given sensation of brightness. The sensation of brightness in question may be that of threshold brightness or of some brightness above the threshold. It may now be assumed that equal brightness means that an equal number of quanta has been absorbed by the visual purple no matter what the wavelength of the stimulating light.

14. von Grotthus, T.: Abhandlungen über Elektrizität und Licht, in Ostwald, F. W.: Klassiker der exakten Wissenschaften, Leipzig, Wilhelm Engelmann, 1906, no. 152, p. 101.

15. Draper, J. W.: On Some Analogies Between the Phenomena of the Clinical Rays and Those of Radiant Heat, Phil. Mag. **19**:195, 1841; On the Allotropism of Chlorine as Connected with the Theory of Substitutions, ibid. **27**:327, 1845.

16. Einstein, A.: Ueber einen die Erzeugung und Verwandlung des Lichtes betreffenden heuristischen Gesichtspunkt, Ann. d. Phys. **17**:132, 1905; Thermodynamische Begründung des photochemischen Aequivalentgesetzes, ibid. **37**:832, 1912; Nachtrag zu meiner Arbeit: "Thermodynamische Begründung des photochemischen Aequivalentgesetzes," ibid. **38**:881, 1912.

17. Stark, J.: Weitere Bemerkungen über die thermische und chemische Absorption im Bandenspektrum, Physikal. Ztschr. **9**:889, 1908; Ueber die zerstäubende Wirkung des Lichtes und die optische Sensibilisation, ibid. **9**:894, 1908.

18. Dartnall, H. J. K.; Goodeve, C. F., and Lythgoe, R. J.: The Effect of Temperature on the Photochemical Bleaching of Visual Purple Solutions, Proc. Roy. Soc., London, s.B **136**:35, 1937.

If I_o is the incident energy, I_a the energy absorbed by the visual purple, a the absorption coefficient of visual purple and c the concentration of visual purple, then Beer's law may be expressed as follows:

$$(1)\ I_a = I_o\ (1 - e^{-ac}).$$

One can express e^{-ac} by expanding it into the series:

$$(2)\ e^{-ac} = 1 - ac - \frac{a^2c^2}{2!} \ \ldots\ .$$

With small values of c, the terms with powers higher than the first may be neglected. Substituting equation 2 in equation 1, one gets:

$$(3)\ I_a = I_o\, ac \text{ or } a = \frac{I_a}{I_o c}$$

Now the number of incident quanta, n_o, is proportional to the incident energy for any given wavelength. That is,

$$(4)\ n_o = kI_o.$$

Also, the number of absorbed quanta, n_a, is proportional to the absorbed energy, and since the absorbed energy is of the same wavelength as the incident energy, the constant of proportionality remains k, so that

$$(5)\ n_a = kI_a.$$

Dividing equation 5 by equation 4 gives

$$(6)\ \frac{I_a}{I_o} = \frac{n_a}{n_o},$$

and substituting this in equation 3 gives

$$(7)\ a = \frac{n_a}{n_o c}$$

But, as has been seen, in the experimental conditions under which the visibility curve is determined, the value of n_a at every wavelength is the same, since sensations of equal brightness are produced at every wavelength. Also, the concentration, c, is the same at every wavelength, since the state of adaptation is constant. Expressing $\frac{n_a}{c}$ as a new constant, k', gives

$$(8)\ a = \frac{k'}{n_o},$$

which states that the absorption coefficient in inversely proportional to the number of incident quanta necessary at each wavelength to produce a given sensation of brightness. Now the usual visibility curve plots the reciprocal of the amount of energy necessary to produce a given sensation of brightness at each wavelength, i. e., visibility$=V=1/I_o$; but since the value of I_o and the wavelength are known, visibility may equally well be expressed as the reciprocal of the number of quanta necessary to produce a given sensation of brightness at each wavelength, i. e.,

$$(9)\ V = \frac{1}{n_o}$$

and substituting equation 9 in equation 8 gives

$$(10)\ a = k'V,$$

which states that the absorption coefficient of rhodopsin at any wavelength is proportional to the visibility expressed in quantum terms

at that wavelength. The values of α for various values of λ (wavelength) are known for visual purple. The values of $1/I_0$ for various values of λ are also known; and, indeed, these values determined at low intensities are the data which are plotted in the scotopic ocular visibility curve. The first task is to transform the scotopic ocular visibility curve, by means of the data which E. F. McCarthy and I obtained on the absorption spectrum of the refractive media of the human eye, into a scotopic retinal visibility curve. The observers used by Hecht and Williams in their determination of the visibility curve had an average age of "about 25 years." Therefore, E. F. McCarthy and I computed the average absorption spectrum for the refractive media of four eyes with an average age of 21.5 years, as described in a previous paper.[10] The scotopic ocular visibility curve was now transformed by utilizing this average selective absorption data. The result of this transformation is that the visibility curve is expressed in terms of energies incident on the retina rather than in terms of energies incident on the cornea. Taking the reciprocals of the energies incident on the retina necessary to produce a given sensation of brightness gives the scotopic retinal visibility curve.

Now a further transformation is needed. The scotopic retinal visibility curve as found by the foregoing method is expressed in terms of energies; but, according to the Stark-Einstein law the number of molecules decomposed in a photochemical reaction is proportional not to the amount of energy absorbed but to the number of quanta absorbed. Since the quantum energy varies with the wavelength, a further transformation must be made in order to express the scotopic retinal visibility curve in terms of quanta, i. e., it is necessary to know the reciprocal of the number of quanta required at each wavelength to produce a given sensation of brightness. This transformation is readily accomplished by dividing the necessary incident energy at each wavelength by the quantum energy at that wavelength. This gives the number of quanta necessary at each wavelength to produce a given sensation of brightness. Taking the reciprocal of each such number gives the scotopic retinal visibility curve expressed in terms of quanta. The total effect of both transformations is shown in chart 3. The scotopic visibility curve after both transformations is much higher than the transformed curve in the blue end of the spectrum, and its peak, as determined by several methods of interpolation, is shifted more than 10 millimicrons toward the violet end of the spectrum. Only 3 millimicrons of this shift can be attributed to the Stark-Einstein effect. Chart 4 shows the scotopic retinal visibility curve expressed in terms of quanta as compared with the absorption coefficients of rhodopsin. Since all that is necessary is that the absorption coefficients of rhodopsin should be proportional to the scotopic

retinal visibility curve in terms of quanta, it is legitimate to give both curves the same maximum ordinate, and this has been done. It is to be seen that chart 4 shows a much greater degree of agreement between the two curves than does chart 2. The comparison made by Hecht and Williams, shown in chart 1 is, of course, not adequate because (1) they did not have available to them the modern data on the absorption spectrum of rhodopsin; (2) they did not have available to them the data on the absorption spectrum of the ocular media; (3) they failed to utilize the data of Koettgen and Abelsdorff in the blue end of the spectrum, where disagreement would have been evident, and, finally, (4) they failed to make the necessary Stark-Einstein transformation. Chart 4 shows that the maxima of the two

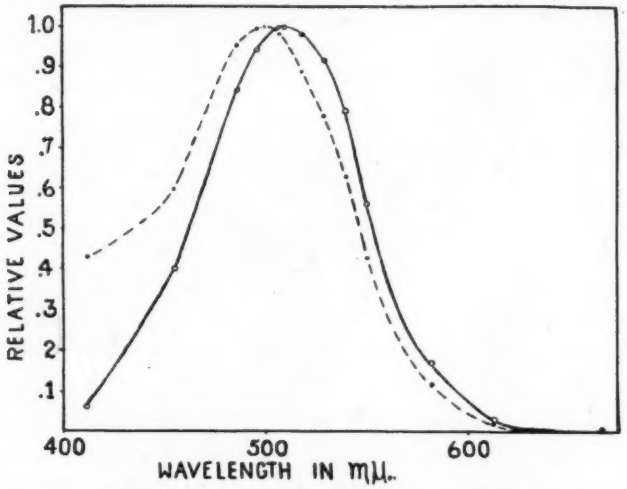

Chart 3.—The solid line is the scotopic ocular visibility curve in terms of energies (Hecht and Williams); the dash line, the scotopic retinal visibility curve in terms of quanta (Ludvigh).

curves are almost coincident. The difference between the maxima of the two curves has been reduced from over 9 millimicrons to less than 1 millimicron. The determination of the maximum for each of the curves is subject not only to experimental error but to sampling error. Furthermore, the maximum in each case must be found either by interpolation or by means of an equation giving an empiric fit for the values in the vicinity of the maximum. In view of these sources of error, it may be concluded that the difference of less than 1 millimicron between the maxima of the two curves of chart 4 is not significant.

The foregoing considerations lead to the conclusion that it is unnecessary to invoke Kundt's rule to explain the discrepancy between

the maximum of the absorption spectrum of rhodopsin and the maximum of the scotopic visibility curve, because any significant discrepancy disappears when the comparison between the two sets of data is properly made. Since it is a priori improbable that Kundt's rule is operating, and since there is no discrepancy between the maxima left for it to explain, it may be concluded that Kundt's rule is not applicable to visual purple under the conditions in question. Hecht and Williams have suggested that the Kundt shift may account for the difference between the scotopic and the photopic visibility curve. But if the Kundt shift does not account for the difference of 9 or 10 millimicrons between the maxima of the two curves shown in chart 2, then it seems unlikely that it accounts for the difference of

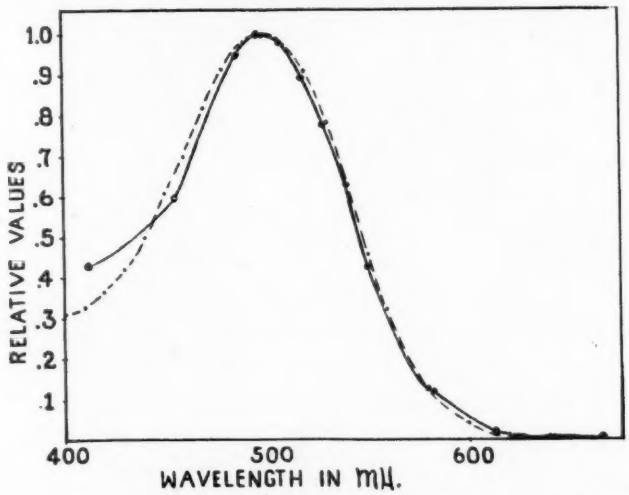

Chart 4.—The solid line is the scotopic retinal visibility curve in terms of quanta (Ludvigh); the dash line, the absorption spectrum of visual purple (Lythgoe).

almost 50 millimicrons between the scotopic and the photopic visibility curve.

The height of the scotopic retinal visibility curve at wavelengths less than 430 millimicrons indicates that the eye is more sensitive to light of these short wavelengths than would be expected from the absorption spectrum of visual purple. Three possible explanations for this discrepancy are suggested: 1. The selectivity of the absorption by the refractive media of the young human eye may not be so great as the calculations made by E. F. McCarthy and me indicate for the reasons discussed in a previous paper.[10] 2. Strong fluorescence by the retina might make the apparent sensitivity of the eye to light of short wavelengths greater than it actually is. In our determination of the absorption spectrum of the refractive media of the human eye

while the media were in situ in the eye, the retina was not included. 3. The presence of stray light may cause the measured sensitivity of the eye to light of short wavelengths to be considerably greater than its true sensitivity. Hecht and Williams in determining the scotopic ocular visibility curve do not appear to have taken any precautions to exclude this factor. Stray light may in part account for the different results obtained by different observers [19] when working at short wavelengths.

There are several interesting conclusions to be drawn from chart 4. One conclusion depends on the fact that the scotopic retinal visibility curve expressed in terms of quanta is clearly unsymmetric and not well fitted by a one term exponential formula. The high degree of symmetry of the scotopic ocular visibility curve expressed in terms of energies and also the accuracy with which it may be fitted by a simple probability equation have led several authors [20] to suggest that these two facts are of importance for a theory of vision. Thus Hecht and Williams [2] and Hecht [1d] noted that the scotopic ocular visibility curve is symmetric and that Nutting's [21] formula for the similar photopic ocular visibility curve is based on a probability function. Hecht assumed that "the absorption coefficient of the sensitive substance in the eye will be proportional to the reciprocal of the amount of energy needed to produce a given brightness in the eye." Then the absorption spectrum of visual purple will also be symmetric. This assumed symmetry Hecht and Williams explained by a further hypothesis. They stated: "The symmetrical or nearly symmetrical curves that represent simple absorption spectra resemble strikingly the distribution curves of errors, of population, etc., which are familiar in the theory of statistics. It may be that the shape of an absorption curve represents the fact that the absorbing substance is composed not of a uniform series of resonators, but of a group of resonators whose free periods may be expressed by the common distribution curves

19. Hartman, L. W.: The Visibility of Radiation in the Blue End of the Visible Spectrum, Physiol. Rev. **11**:327, 1918. Coblentz, W. W., and Emerson, W. B.: Relative Sensibility of the Eye to Light of Different Colors and Some Practical Applications to Radiation Problems, Bulletin 14, United States Department of Commerce, Bureau of Standards, 1918, p. 167. Nutting, P. G.: The Visibility of Radiation, Phil. Mag. **29**:301, 1915.

20. (*a*) Priest, I. G.: The Law of Symmetry of the Visibility Function, Physiol. Rev. **11**:498, 1918. (*b*) Troland, L. T.: The Enigma of Color Vision, Am. J. Physiol. Optics **2**:23, 1920; (*c*) The Nature of the Visual Receptor Process, J. Optic. Soc. America **1**:3, 1917; (*d*) Brilliance and Chroma in Relation to Zone Theories of Color, ibid. **6**:3, 1922. (*e*) Hecht.[1d] (*f*) Hecht and Williams.[2]

21. Nutting, P. G.: The Luminous Equivalent of Radiation, Bulletin 103, United States Department of Commerce, Bureau of Standards, 1908, p. 261.

of the statisticians." But, as has been shown, the absorption spectrum of visual purple should resemble not the scotopic ocular visibility curve expressed in terms of energies but the scotopic retinal visibility curve expressed in terms of quanta. Furthermore, since the latter curve is asymmetric, any explanation of its symmetry, whether by means of a population distribution of the free periods of a group of resonators or otherwise, is superfluous.

Prior to the work of Hecht and Williams, Troland [20b] drew from the symmetry of the visibility curve a conclusion opposite to that of Hecht and Williams. He stated: "This extreme symmetry of the visibility curve seems to me to militate somewhat against chemical theories of the visual receptor process. Resonance curves, in general, are asymmetrical; and the same is true of absorption curves, which are particular examples of resonance curves. None of these curves fit the probability function." The knowledge that the scotopic retinal visibility curve expressed in terms of quanta is markedly asymmetric both eliminates the objection of Troland and makes unnecessary the assumption of Hecht and Williams.

Another important conclusion to be drawn from the agreement between the corrected visibility curve and the absorption spectrum of visual purple concerns the question of the "purity" of solutions of visual purple. Thus the results of Lythgoe,[5] of Krause and Sidwell [6] and of Bayliss, Lythgoe and Tansley [7] all show that the absorption spectrum of the visual purple solutions which they used was asymmetric and higher than the scotopic ocular visibility curve in the blue end of the spectrum, as appears in chart 2. This asymmetry was thought to be inconsistent with the scotopic visibility curve and was attributed to the presence of yellow impurities. Thus Bayliss, Lythgoe and Tansley stated in connection with the yellow impurities: "If it were possible to make a full correction for these substances, it is probable that the absorption curve of visual purple would be roughly symmetrical when plotted to a scale of wavelengths." Lythgoe also noted that the absorption of visual purple is relatively high in the blue end of the spectrum and attributed this to yellow impurities, although the better solutions "contain only a small amount of yellow impurities. . . ." He stated that "with successive purifications the density of the unbleached extract becomes progressively less at any one of the short wavelengths" and "with a quite pure extract it would probably be very small in the region of 400 $\mu\mu$. The present solutions almost certainly contain yellow impurities, and before one can derive values for the density of visual purple at the shorter wavelengths, it is necessary to assume values for the absorption of these impurities." Lythgoe, after making allowance for the assumed values

of the absorption spectrum of the yellow impurities, found the absorption spectrum of the "parent" visual purple, which is seen to be roughly symmetric. Granit and Munsterhjelm [22] compared the height of the b wave of the frog's electroretinogram with Lythgoe's data on the absorption spectrum of the "parent" visual purple and observed that "the curve for the b wave extends too far towards the violet end to fit the curve for pure visual purple." They pointed out "the necessity of finding some substance other than visual purple or a modification of visual purple in order to explain the presence of asymmetrical curves."

But, as has been shown, the scotopic retinal visibility curve expressed in terms of quanta agrees not with the absorption spectrum of Lythgoe's assumed "parent" visual purple but with his experimental data uncorrected for the presence of yellow impurities. In view of the fact that Lythgoe's uncorrected data are in agreement with those of Krause on bovine visual purple, it appears that the photosensitive substance involved in scotopic vision is not the calculated "parent" visual purple described by Lythgoe but visual purple in the form in which he actually measured its absorption spectrum. If the absorption spectrum of visual purple is due in part to yellow impurities, then these impurities must also be photosensitive. Another point to be noted is that the data of Granit and Munsterhjelm on height of the b wave agree much more closely with the absorption spectrum of visual purple than they do with that of the hypothetic "parent" visual purple. Therefore, it would seem that the solutions of visual purple obtained by Lythgoe and also those obtained by Krause and Sidwell are indeed practically pure and do not contain nonphotosensitive impurities to any marked extent.

Examination of chart 3 shows that at low intensities the retina is much more sensitive to light of short wavelengths than has commonly been supposed. This fact should be considered in relation to the blue arc phenomenon [23] and also to any theory of color vision which attributes the sensation of blue to the operation of the rods.[24] The significance of the scotopic retinal visibility curve for theories of color vision will be considered more fully in a subsequent communication dealing with the photopic retinal visibility curve.

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22. Granit, R., and Munsterhjelm, A.: The Electrical Responses of Dark-Adapted Frog's Eyes to Monochromatic Stimuli, J. Physiol. **88**:436, 1937.

23. Newhall, S. M.: The Constancy of the Blue Arc Phenomenon, J. Optic Soc. America **27**:165, 1937.

24. Roaf, H. E.: Influence of Coloured Lights on Sensitivity of Eye to Various Regions of the Spectrum: Study in Relation to Theories of Colour Vision, Quart. J. Exper. Physiol. **18**:243, 1927; Colour Vision, Physiol. Rev. **13**:43, 1933.

SUMMARY

A scotopic ocular visibility curve expressed in terms of energies is transformed into a scotopic retinal visibility curve expressed in terms of energies by utilizing experimental determinations of the selective absorption of light by the refractive media of the human eye.

This scotopic retinal visibility curve expressed in terms of energies is then transformed into a scotopic retinal visibility curve expressed in terms of quanta by application of the Stark-Einstein law of photochemical equivalence.

The curve thus obtained is asymmetric and agrees with that representing the modern determination of the absorption spectrum of visual purple.

The significance of the scotopic retinal visibility curve is briefly discussed with respect to Kundt's rule, the Purkinje phenomenon, the purity of visual purple solutions, the b wave of the electroretinogram and certain visual theories.

PHYSIOLOGIC AND CLINICAL OPHTHALMOLOGIC PROBLEMS IN RELATION TO INDIVIDUAL VARIABILITY

A. BRÜCKNER
BASEL, SWITZERLAND

(Continued from page 541)

CONGENITAL COLOR DEFICIENCIES

In a minority of persons the form of color vision hitherto discussed, with the exception of a few individual variations which do not detract from its general character, is not applicable. These are the so-called color defectives—of whom, as modern investigations show, several types are distinguishable.

The majority of recent authors agree that besides the true partly color blind, who do not perceive certain definite colors, e. g., red and green, there are persons who are able to perceive all color qualities but whose color sense is, nevertheless, different from that of the normal person. These are called anomalous.

Concerning the vision of the congenitally color blind: It is generally accepted that it is impossible to conclude from the fact that they correctly name the colors of certain objects that they experience the same color sensations as do normal persons. The color blind have from childhood heard definite things in their surroundings called by definite names, and these names have become impressed on their minds, so that it is natural that they should use them. However, it is by no means certain that their sensations are identical with those of normal persons looking at the same things. The color-blind person probably perceives with greater subtlety than the normal person slight differences in the brightness and saturation of colors. Therefore, a person's color sense cannot be determined only by the results obtained when he names colors presented to him.

To classify persons according to their differentiation of the colors in the spectrum, for instance, is also wrong in my opinion. I emphasize this point, since Edridge-Green,[34] for instance, has classified persons as to their color sense into seven classes, according to the different hues which they discern in the spectrum. The one who sees but a single color is monochromatic; the one who distinguishes two colors is dichromatic; the one who sees seven colors in the spectrum, according to those of

34. Edridge-Green, F. W.: Classification of the Colour-Blind, Ophth. Rev. **35**: 10, 1916.

Newton, is heptachromatic, that is has normal color sense. Among these the anomalous are included, despite the fact that the intensity of light, according to the Bezold-Brücke phenomenon, must influence the number of colors discriminated.

Partial Color Blindness.—The color-blind subject, in contrast to the normal person, who needs three lights for the establishment of all the hues of the spectrum, can perceive all spectral hues by mixing only two—one of each half of the spectrum. Therefore, the person who is color blind is called a dichromat; the normal person, a trichromat. This name is based not on the quantity of sensations but on the number of lights necessary for mixing all the hues.

Probably the person who is color blind sees only blue and yellow in addition to the white-black sensations. The long wave half of the spectrum appears yellow; the other half, blue. Between them is a so-called neutral point, probably uncolored, where the normal person sees the pure green.

As I have already observed, the gaging of the color sense of color-blind persons is possible by means of two lights. Such gaging curves have been obtained by a great number of research workers. I shall cite only König and Dieterici, von Kries,[35] Tscherning and Larsen,[36] Tschermak[37] and von Brücke and Inouye.[38] The curves obtained by König and Dieterici are seen in figure 14. There are two sharply distinct types. Persons with these types were formerly called red blind and green blind. Now they are ordinarily designated protanopes and deuteranopes, according to the terminology of von Kries. The names formerly used may suggest that the one group is blind only for red and the other for green, though both probably are not able to perceive either red or green and see all colors only as yellow or blue of different brightness and saturation. As figure 14 shows, the two curves coincide in the part of the spectrum made up of short waves, but not in that made up of long waves. The same holds true for the curves of von Kries (fig. 15).

The maximum of the warm curve (fig. 14), that is, the part of the spectrum made up of long waves, is situated between 550 and 560 milli-

35. von Kries, J.: Die Gesichtsempfindungen und ihre Analyse, Leipzig, Veit u. Comp., 1882.

36. Tscherning, M., and Larsen, H.: Les anomalies des couleurs, J. de physiol. et de path. gén. **24**:475, 1926; La vision des couleurs, ibid. **24**:492, 1926.

37. Tschermak, A.: Ueber spektrale Verteilung der Sättigung und über Dreilichter-Eichung des Spektrums, Arch. f. Augenh. **109**:1, 1935.

38. von Brücke, E. T., and Inouye, W.: Ueber die Anordnung der homogenen Lichter auf der Mischlinie des Rotgrünblinden mit unverkürzten Spektrum, Arch. f. d. ges. Physiol. **141**:573, 1911.

microns for the protanopes and between 570 and 580 for the deuteranopes, while the maximum of the cold curve, the part of the spectrum made up of short waves, for both groups is to be found at 450 millimicrons.

From these curves the following appearance of the spectrum for the dichromats has been suggested: There is in about the middle of the spectrum a noncolored, or neutral, zone, which lies at a different point for each type, namely, for the protanopes at about 495 millimicrons and for the deuteranopes at about 500 millimicrons. But the chief difference is to be found at the red end of the spectrum, which for the protanopes is dark and therefore shortened, while for the deuteranopes it generally has the same brightness as for persons with normal color sense. The saturation increases on both sides of the neutral zone and decreases again toward the ends of the spectrum, as shown in the curves.

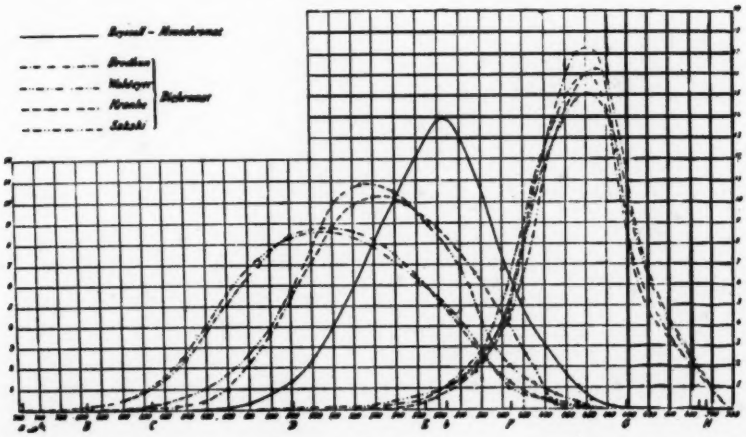

Fig. 14. Gaging curves for dichromats. The curves of Brodhun and Waldeyer are for deuteranopes, and those of Kranke and Sakaki are for protanopes. Beyssell's curve is that of a totally color-blind person. (After König and Dieterici.[27])

Recently Tschermak published a report of experiments which show that the value of the color, or, better, the saturation, does not diminish toward the ends of the spectrum. This finding seems to me to be doubtful. If the curves of König and Dieterici for dichromatic vision are transformed in the same manner that I described for normal color vision, their course does not agree with Tschermak's suggestion. The mean curve for the dichromats is shown in figure 16, in which the continuous line represents the protanopes and the dotted line the deuteranopes.

If Hering's antagonistic theory is right, the areas of yellow and blue for the dichromats should be equal. Apparently this is not so, perhaps for the same reason that I have already discussed, in con-

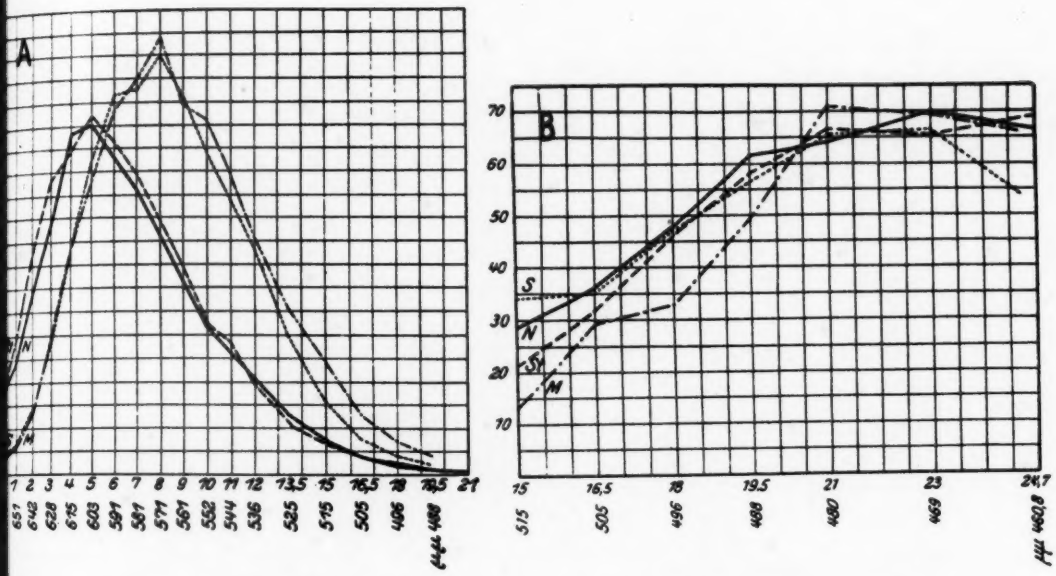

Fig. 15.—*A*, distribution of the red values in the dispersional spectrum of gaslight for 2 protanopes (*S*, indicated by the dotted line; *M*, by the dash and dot line) and for 2 deuteranopes (*N*, indicated by the continuous line; *St*, by the dash line). *B*, distribution of the blue values in the dispersional spectrum of gaslight for 2 protanopes (*S*, indicated by dotted line; *M*, by dot and dash line) and for 2 deuteranopes (*N*, indicated by a continuous line; *St*, by a dash line). (After von Kries, J.: Ueber Farbensysteme, Ztschr. f. Psychol. **13**:241, 1897.)

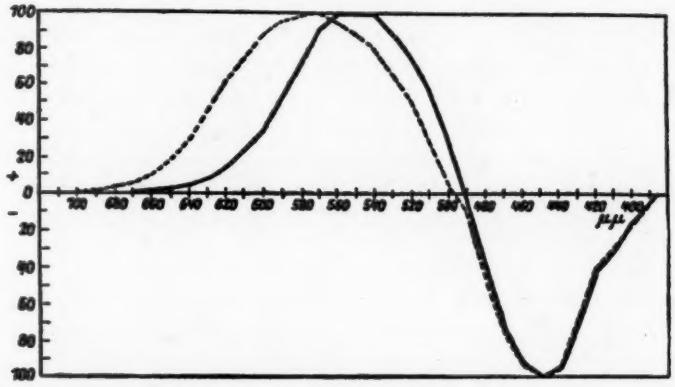

Fig. 16.—König's gaging curves for dichromats transformed into Hering's curves. The continuous line is for a person who is red blind; the dash line is for a person who is green blind. (After Brückner.[80])

nection with the curves of normal color vision, namely, the yellow-reddish character of the daylight or the influence of diascleral light.

Anomalous Trichromats.—The group of anomalous trichromats was first discovered by Lord Rayleigh [28c] in 1881. They need three gaging lights in order to produce all hues; hence their name, anomalous trichromats. Lord Rayleigh investigated color equations by a mixture of a spectral red of 670 millimicrons (a line of lithium) and a spectral yellowish green of 530 millimicrons (a line of thallium), which appears equal to the yellow of 589 millimicrons, the line of sodium. The proportions of the two components required to reach an equation was nearly the same. A few of his observers required more green, and a few, more red. Mixed lights prepared to meet the requirements of these groups were naturally too green or too red for normal persons. Further experiments by Donders [29] and von Kries confirmed this result.

The terminology is at best a little complicated. At first the group which needs more green was called green anomalous; the other, red anomalous. Then von Kries introduced the term protanomal for those who need more red and deuteranomal for those who require more green in the test equation named the Rayleigh-Donders equation.

When tests are made some anomalous are found who not only accept a strictly definite proportion of the two mixed lights of 670 and 530 millimicrons but who accept with the homogeneous yellow light of 589 millimicrons a larger amount of different proportions of the two other lights when the luminosity of the yellow light alone is correspondingly altered. Some of them accept the equation of pure yellow and pure green, or of yellow and pure red. They were called the extreme deuteranomals or protanomals. Probably they represent transition types between the normal and the color blind. But it seems necessary to gage the whole system of these types and not to limit the test to the single Rayleigh-Donders equation, as has hitherto usually been done for persons with these extreme forms of anomaly.

Originally, the anomalous were looked on merely as a theoretically interesting variety. The detailed investigations by Nagel [39] and Guttmann [40] at the beginning of the century proved that these so-called anomalous trichromats are in many respects defective. They have always higher specific thresholds than normal persons. They require a larger stimulus, in the form of increased size of field, intensity of light, saturation or duration. For instance, a small colored field can be perceived by the anomalous at a shorter distance than by normal persons.

This fact of higher thresholds leads to consideration of the anomalous as color defective and therefore to their exclusion from the navy and

39. Nagel, W. A.: Die Diagnose der anomalen trichromatischen Systeme, Klin. Monatsbl. f. Augenh. **42**:366, 1904.

40. Guttmann, A.: Untersuchungen über Farbenschwäche, Ztschr. f. Psychol. u. Physiol. d. Sinnesorg. (Abt. 2) **42**:24 and 250, 1907; **43**:146, 199 and 225, 1908.

the railway service, because there differentiation of colored signals is necessary. In England, as far as I know, these regulations have not been strictly adopted, but in Germany, Switzerland and recently also in France the anomalous are excluded from the railway service.

I shall not go into detail about the results of investigations of the color thresholds of the anomalous. They are only in part satisfactory. I shall confine myself to presenting curves showing the thresholds for the duration of the colored light—*die Farbenzeitschwelle.*

These results were obtained by using a so-called tachistoscope, which allows the exposure of a colored field for a very short fixed time, usually only a few thousandths of a second. The investigation showed that generally the time of the exposure required for the perception of the specific color depends on the luminosity of the screen on which for a moment the colored light appears. The duration is, as will be seen in figure 17, a linear function of the brightness of the screen. Red has the lowest threshold; green, the highest. [41]

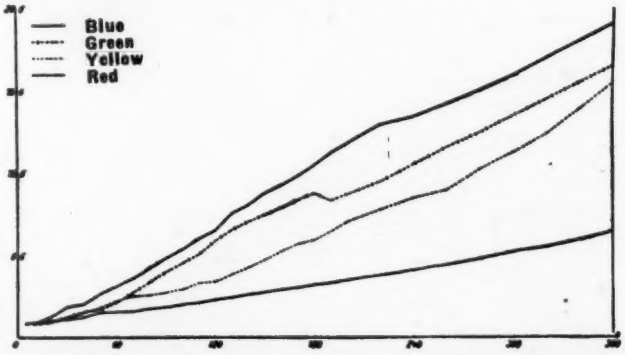

Fig. 17.—Curves of the thresholds for the duration of the colored light in relation to the luminosity of the screen on which the color appears (abscissas). The numbers for the degrees indicate the turbinoid values of gray; 0 equals black; 360, white. The ordinates indicate the time in thousandths of a second (σ) during which the colored field was exposed. (After Brückner and Kirsch.[41])

This fact has already been established by Guttmann, who when using spectral colors found the thresholds much lower than those obtained with pigment colors. He therefore suggested that the former have a higher specific value than the latter. But this explanation is not correct. The differences found by Guttmann are related only to the brightness of the surface on which the colored light appears; in the spectroscope the field is ordinarily very dark, say black. Therefore, in contrast to the other experiments, the thresholds are very low.

The anomalous trichromats have, compared to normal persons, high thresholds for the length of exposure to colored light. This holds especially for green for deuteranomals (fig. 18). Protanomals were not

41. Brückner, A., and Kirsch, R.: Untersuchungen über die Farbenzeitschwelle, Ztschr. f. Psychol. u. Physiol. d. Sinnesorg. (Abt. 2) **46**:229, 1912.

examined by this method. The increase of this one threshold seems to be sufficient ground for excluding the anomalous from the railway service, because mistakes may be followed by disastrous consequences.

Gaging curves for the ordinary forms of anomalous color vision are given by many investigators, e. g., König and Dieterici, Tscherning, Pitt and others. I shall show only the curves of König and Dieterici transformed into curves corresponding to Hering's for pure colors, the coordinates having been altered in the manner already described (figs.

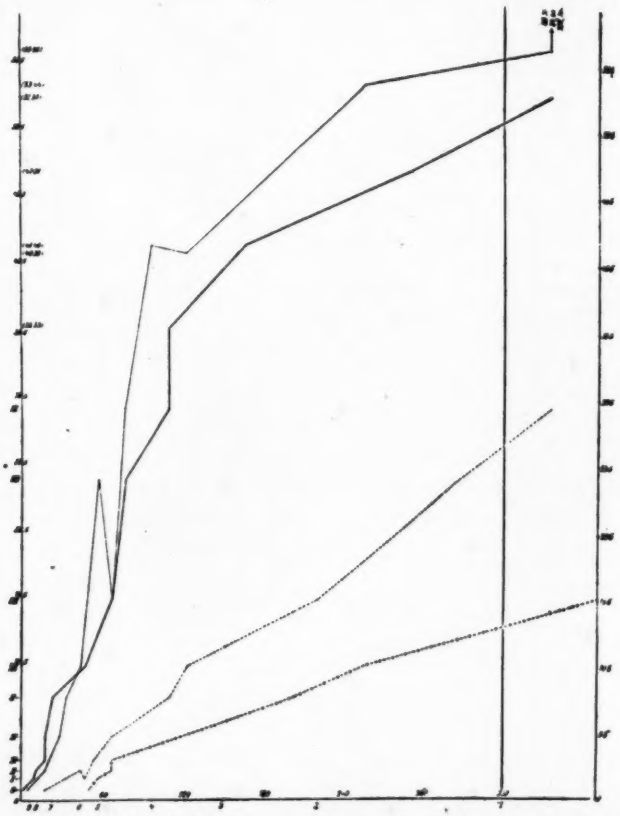

Fig. 18.—Duration thresholds for green of two deuteranomals (continuous lines) and two normal persons (dotted lines). (After Brückner and Kirsch.[41])

11 and 12). It is to be observed that for green the curve of the anomalous is a good deal lower than that of normal persons. This agrees with the fact that in practical life this group is especially deficient in the green color sense. For protanomals the same finding is not yet established by this method, especially with regard to red.[42]

42. I should mention the opinion of Hess, who found, especially in deuteranomals, an increased yellow-blue sensitivity. His results do not appear to be fully convincing.

Of the rare deficiency of color vision for yellow-blue, I shall say only a few words. Some persons with what is described as yellow-blue blindness have also an insufficient red-green sense. This fact suggests that the deficiency in color vision is not congenital but acquired. Yet in some cases it may be congenital, though not necessarily hereditary. In a few cases described recently by Engelking [43] as instances of tritanomalous deficiency the condition was hereditary, as shown by the pedigree. But it seems to me it is not absolutely justifiable to conclude that this anomaly is determined by a genetic cause in the so-called X chromosome, as other forms are supposed to be.

Diagnosis.—For the clinical diagnosis of the disturbances of color sense it is naturally not possible to obtain gaging curves. Simple tests have been used for many decades past. The oldest test is that of Seebeck,[44] who in 1837 suggested the use of color pigments. About fifty years later Holmgren [45] suggested the use of colored wools. The person whose color sense was to be tested was required to match a given color with the other colored wools. From the mistakes in matching the physician drew his conclusions as to the patient's color sense. It is now known that many anomalous trichromats are able to pass this test, apparently because the individual fields are not small enough. The size of the colored field is of the greatest importance for the recognition of colors by the anomalous.

Far better for this purpose are the so-called pseudoisochromatic tables, first used by Stilling and improved by other authors. First place is to be given to the Ishihara test [46] and to the latest editions of the tables of Stilling.[47] In these tables small colored fields of different form and size are printed. In these the confusion colors of the color blind are printed on a card in the form of small spots which are so arranged that normal persons and those who are color blind recognize different figures. For the illiterate there are other cards, with winding lines which the patient is required to trace with a pointer.

Other charts, based on the same principle of pseudoisochromatism, namely colors which falsely seem to the color blind to be the same, have been published by Nagel, Podesta, Schaaff, Pollack and Bostroem. All these tests are much better than the color-matching tests of Holmgren and are more suitable for investigations of school children or for determining the incidence of color deficiency in the population.

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43. Engelking, E.: Die Tritanomalie, ein bisher unbekannter Typus anomaler Trichromasie, Arch. f. Ophth. **116**:196, 1925.

44. Seebeck: Ueber den bei manchen Personen vorkommenden Mangel des Farbensinnes, Ann. d. Phys. u. Chem. **42**:177, 1837.

45. Holmgren, F.: Die Farbenblindheit in ihren Beziehungen zu den Eisenbahnen und der Marine, Leipzig, F. C. W. Vogel, 1878.

46. Ishihara, J.: Test for Colour-Blindness, ed. 7, Tokyo, Japan, Kanehara & Co., 1936.

47. Stilling, J.: Stillings pseudo-isochromatische Tafeln zur Prüfung des Farbensinnes, ed. 18, Leipzig, Georg Thieme, 1929.

These tests are suitable for rapid orientation, and when properly applied hardly a single color-deficient person escapes detection. Nevertheless, I have observed rare cases in which color defect could be detected only by tests with the spectroscope. As to the constitution of the color sense itself, these tests do not reveal much. They determine merely whether or not the person examined has a normal color sense. It is not possible by their use to establish with certainty the type of color defect present.

This may be more exactly diagnosed by the anomaloscope constructed by Nagel [48] for this special purpose. This apparatus,[49] a small spectroscope, is used in Germany, and for the past ten years has been used in Switzerland also, for the examination of all candidates for the railway service. It has been adopted in France during recent years. From experience in Switzerland, where all candidates are examined by Stilling's tables and the anomaloscope, I regard this combined method as completely sufficient.

The anomaloscope (figs. 21 and 22) reproduces the original Rayleigh-Donders equation. The patient is shown a field one half of which is illuminated by a light of 589 millimicrons and the other half by a mixture of lights of 670 and 530 millimicrons. It is therefore easy to determine the two types of anomalous as well as the true color blind. If one uses homogeneous red and homogeneous yellow or green and yellow in the case of color blindness, an equation is obtained by regulating only the luminosity. Therefore, according to the axiom that if two quantities are equal to a third they are equal to one another, it is permissible to suppose that in this case green and red seem equal, as is supposed to be the case in color blindness.

As I have already said, there are two types of persons with color blindness and with color anomaly. The relations between them are not clear. Hering [50] suggested that the protanopes and deuteranopes may be differentiated by different pigmentation of the macula or of the lens. But von Kries rightly denied this, on the ground of the gaging curves. It is now known that they have substantially different systems of color sense. The same holds for protanomals and deuteranomals.

Frequency of the Different Types of Color Deficiency.—As to the frequency of the different types of color deficiency, recent statistical investigations provide reliable information.

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48. Nagel, W. A.: Zwei Apparate für die augenärztliche Funktionsprüfung, Adaptometer und kleines Spektralphotometer (Anomaloskop), Ztschr. f. Augenh. **17**:201, 1907.

49. The anomaloscope is manufactured not only by Schmidt & Haensch, Berlin, but by Optik und Mechanik A. G. in Basel.

50. Hering, E.: Ueber individuelle Verschiedenheiten des Farbensinnes, in Wissenschaftliche Abhandlungen, Leipzig, Georg Thieme, 1931, vol. 2.

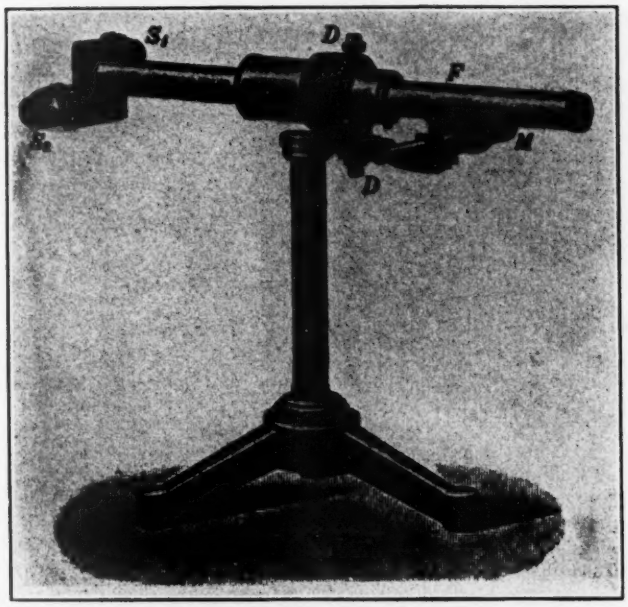

Fig. 21.[54a]—Nagel's anomaloscope. *K* indicates the collimator tube; *D*, the direct vision prism; *B*, the diaphragm; *F*, the ocular tube; *O*, the aperture of the ocular tube through which observation is made; *M*, the screw for changing the situation of the ocular tube, and S_1 and S_2, the slit mechanism. (After Nagel.[48])

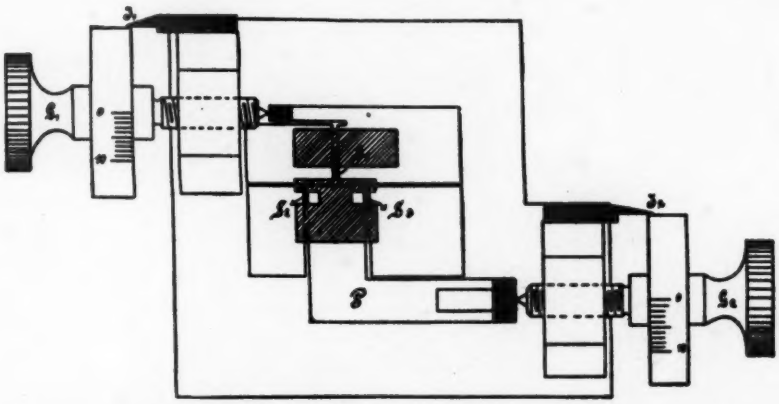

Fig. 22.—Nagel's anomaloscope. View of the slit mechanism. S_1 indicates the slit for homogeneous light of 589 millimicrons; S_2 and S_3, the slits for the red and green lights of the mixed field; G_1 and G_2, screws for changing the width of the slits. (After Nagel.[48])

54a. Figures 19 and 20 have been deleted.

The older statistics not based on the use of the anomaloscope are not satisfactory. I may mention the researches of Waaler [51] in Norway, and those of von Planta,[52] Brunner [53] and Wieland [54] in Basel, carried out in schools. The investigations concern a total of about 11,000 boys and 12,000 girls. As seen in table 2, boys predominate over girls in color deficiency, as was known long ago. The most frequent form is the deuteranomalous and the least frequent the protanomalous, while deuteranopia and protanopia take an intermediate position (table 3).

Heredity of Color Deficiency.—In the population of Europe about 8 per cent of the men are color deficient, but only about 0.4 per cent of the women. This proportion is due to the fact that the heredity of

TABLE 2.—*Frequency of Congenital Color Deficiencies*

Author	Frequency, Percentage	Number Examined	Mean Error
	In Boys		
Waaler	8.01	9,049	±0.29
von Planta	7.95	2,000	±0.37

Author	Theoretic Frequency, Percentage	Actual Frequency, Percentage	Number Examined	Mean Error
	In Girls			
Waaler	0.642	0.44	9,072	±0.07
von Planta	0.631	0.43	3,000	±0.12

TABLE 3.—*Frequency of the Different Types of Congenital Color Deficiency in Boys*

	Color Deficiency	Results of Waaler, Percentage	Results of von Planta, Percentage
a	Protanope	0.88	1.60
b	Protanomal	1.06	0.60
c	Deuteranope	1.04	1.50
d	Deuteranomal	5.06	4.25
	Total	8.01	7.95

color deficiency is sex-linked recessive, that is to say, it is bound to the so-called X chromosome.

The regular form of sex-linked heredity is transmitted by the phenotypically normal woman from her affected father to some of her sons (fig. 23). The daughters also are partially genotypically normal,

51. Waaler, G. H. M.: Ueber die Erblichkeitsverhältnisse der verschiedenen Arten von angeborener Rot-Grünblindheit, Acta ophth. **5**:309, 1927; Ztschr. f. indukt. Abstammungs- u. Vererbungsl. **45**:279, 1927.

52. von Planta, P.: Die Häufigkeit der angeborenen Farbensinnstörungen bei Knaben und Mädchen und ihre Feststellung durch die üblichen klinischen Proben, Arch. f. Ophth. **120**:253, 1928.

53. Brunner, W.: Ueber den Vererbungsmodus der verschiedenen Typen der angeborenen Rotgrünblindheit, Arch. f. Ophth. **124**:1, 1930.

54. Wieland, M.: Untersuchungen über Farbenschwäche bei Konduktorinnen, Arch. f. Ophth. **130**:441, 1933.

partly affected but phenotypically also normal. There can be a color-deficient daughter only when both X chromosomes are affected.

This fact naturally suggests the necessity to investigate the relation between the different types of deficiency for red-green sensations,

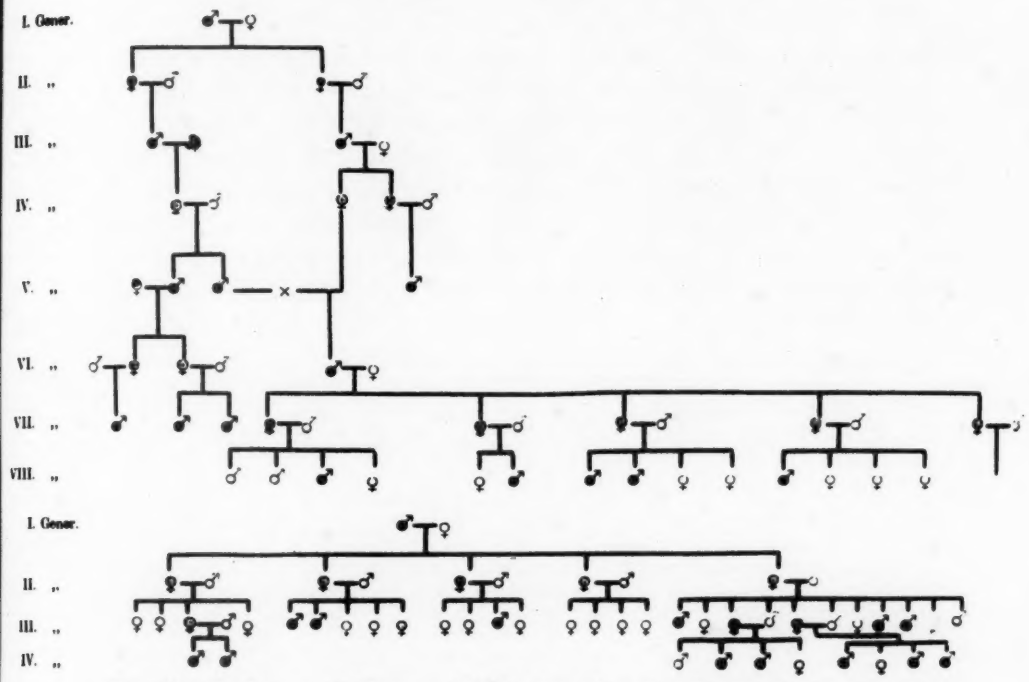

Fig. 23.—Pedigrees of Horner (1876); heredity of red-green blindness. The black circle indicates a color-blind person; the circle with a dot in the center, a woman transmitting the defect; a white circle, a normal person, and *X*, marriage of a color-blind man and a woman transmitting color blindness; ♂ indicates male and ♀, female. (After Franceschetti, in Schieck, F., and Brückner, A.: Kurzes Handbuch der Ophthalmologie, Berlin, Julius Springer, 1930.)

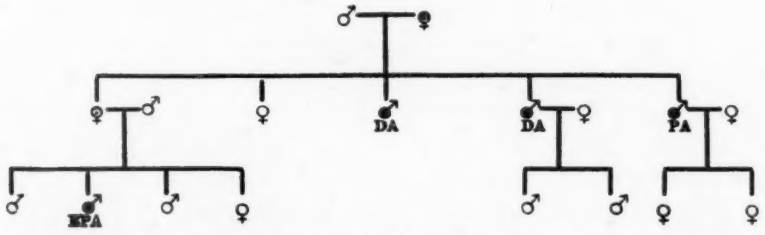

Fig. 24.—Appearance of deuteranomaly and protanomaly in the same family. (After Brunner.[53]) *DA* indicates deuteranomaly; *PA*, protanomaly, *EPA*, extreme protanomaly.

especially to determine if there is a closer connection between deuteranopes and deuteranomals, on the one hand, and between protanopes

and protanomals, on the other hand. Here the works of Waaler and Brunner have enriched knowledge remarkably.

Waaler expressed the opinion that the protanopes and the deuteranopes are genetically different. He published some pedigrees which supported this suggestion, and Brunner pursued these investigations still further. I shall discuss only a few important points of these results.

As already noted, a female will be color blind if both X chromosomes are affected by the gene of color deficiency. If one of them is affected by the factor for protanopia and the other by that for deuteranopia and these two are not so-called allelomorphs, the child cannot be color blind. Waaler called them compounds. The pedigree in figure 24 shows that a phenotypically normal woman has color-deficient sons of both types, which can be explained only if one supposes that the two genes for different forms of color deficiency split off into the different forms in the sons.

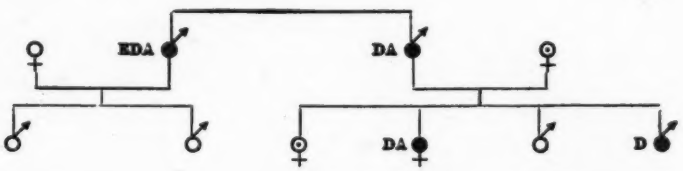

Fig. 25.—Appearance of different degrees of color deficiency in the same family. *D* indicates deuteranopia; *DA*, deuteranomaly; *EDA*, extreme deuteranomaly. (After Brunner.[53])

A pedigree like this abolishes the former suggestion of Hering that the two types of protanopes and deuteranopes are produced only by subordinate or physical differences. One must suppose that these two types are fundamentally genetically different or, according to Morgan, that the locus of their genes in the chromosome is different.

A second fact of some importance is obvious from the pedigree (figs. 25 and 26). There are in the same family persons with different degrees of color deficiency, for instance, deuteranopes and deuteranomals or deuteranopes and extreme deuteranomals. As far as heredity is concerned, it is of interest that the deficiency of a lower degree always dominates over that of a higher degree. But it must not be forgotten that the diagnosis in all these cases was made by testing by the Rayleigh-Donders equation alone. Therefore, it is not known what gaging or measurement of the color thresholds would show.

Nevertheless, it is conceivable that in respect to heredity there may be quantitative differences in the gene for color sense. How this is to be explained is still uncertain, but perhaps the same circumstances are valid as hold good in regard to the heredity of sex, according to Goldschmidt.

In this connection I may refer to some investigations carried out in the ophthalmologic clinic of Basel by Wieland [54] and Meister [55] concerning the color thresholds. Fleischer [56] observed that the color sense of women who transmit color deficiency was sometimes slightly deficient, although it had hitherto been considered normal. But Fleischer did not determine this by precise methods. Wieland and Meister used an apparatus constructed by Pulfrich of the house of Zeiss at Jena, the so-called *Stufenphotometer*. This apparatus allows manifold applications, especially in the investigation of color thresholds.

Two of Ostwald's small colored cards were used as a pure red and pure green. In addition, the light reflected by a gray card of the same brightness as the colored one was exactly measured in order to determine the amount of green or red necessary to permit appreciation of the color. These experiments showed that for normal persons 5 to 6 per cent of red and 10 to 17 per cent of green was necessary. For the anomalous the thresholds were considerably raised; for green, 30 per cent or more.

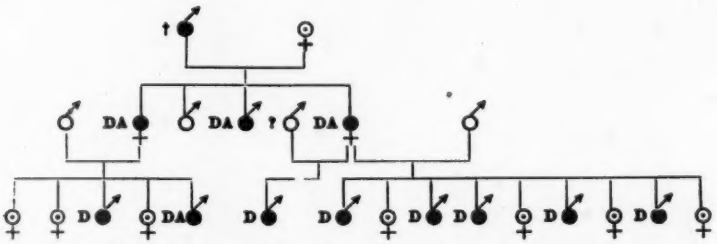

Fig. 26.—Occurrence of deuteranopia (*D*) and deuteranomaly (*DA*) in the same family. (After Brunner.[53])

But women who transmitted color deficiency, irrespective of the form of deficiency they transmitted, had a remarkable increase in the threshold for red and still more in that for green. This is true also of the mathematical evaluation of errors.

The conclusion seems justified that even in the apparently normal woman who transmits deficiency, slight deficiency in color vision is present. Study of heredity has shown similar phenomena, for instance concerning the apparently dominant color of some flowers. These examples suggest that there is some deficiency in the gene for color vision of the one who transmits deficiency.

I believe that exact investigation of color thresholds will elucidate many points that are still doubtful. But for the present it may be

55. Meister, H.: Untersuchung spezifischer Schwellen mittels des Pulfrichschen Stufenphotometers, Ztschr. f. Sinnesphysiol. **65**:217, 1934.

56. Fleischer, B.: Ueber die Vererbung geschlechtsgebundener Krankheiten, Ber. ü. d. Versamml. d. deutsch. ophth. Gesellsch. **42**:4, 1920.

stated that the majority of persons having normal color sense are supplied with such an amount of hereditary mass responsible for this visual function that small differences in color vision do not produce a remarkable difference of reaction in practical life. Apparently a much larger deficiency in the X chromosome is necessary to produce the ordinary characteristic types of alteration of color sense. Perhaps in such cases some remains of genetic substance may exist, and therefore the deficient persons may have a slight faculty, for instance, for perceiving red. Some statements of Nagel [57] and other authors who were themselves color blind seem to suggest this. However, the two great groups of protanopes and deuteranopes certainly persist, and transition types between them do not occur.

Research in genealogy has also demonstrated that the opinion of Georges Elias Müller [58] is not quite justified. He supposed the anomalous to represent altered systems of color vision, *Alterationssysteme,* their character being only a slightly different reaction to colored lights. In some sense he may be right. But with regard to heredity research has shown that the scientific standpoint must be changed and that genetically determined differences do exist.

Many questions are as yet insufficiently investigated, especially the exaggerated contrast of the anomalous, which I shall discuss later.

Total Color Blindness.—Only a few comments need be made about congenital total color blindness. Persons with such a defect are not able to perceive colors; they see only black, gray and white. It is possible to produce excitation for all these colors by changing the intensity of only a single homogeneous light. Therefore, the persons are called monochromats. To them the brightness of the different parts of the spectrum or of other colors does not appear at all as it does to normal persons or to deuteranopes; to the totally color blind they appear exactly as the different colors or parts of the spectrum appear to the normal dark-adapted eye.

Total congenital color blindness is, as shown by the study of pedigrees, a recessive hereditary condition (fig. 27). The eye which has a much diminished visual acuity—not more than a tenth or a seventh of normal vision—is dazzled by light and has nystagmus. Dark adaptation is not diminished, but apparently light adaptation is. Figure 28 shows the typical behavior of a totally color-blind child in daylight.

If it is supposed that in such an eye only the dark adaptation apparatus functions, and since only cones are to be found in the human macula, the reduction of visual acuity is explained, because the normal

57. Nagel, W.: Farbenumstimmung beim Dichromaten, Ztschr. f. Psychol. u. Physiol. d. Sinnesorg. (Abt. 2) **44**:5, 1909.

58. Müller, G. E.: Darstellung und Erklärung der verschiedenen Typen der Farbenblindheit, Göttingen, Vanderhoed & Ruprecht, 1924.

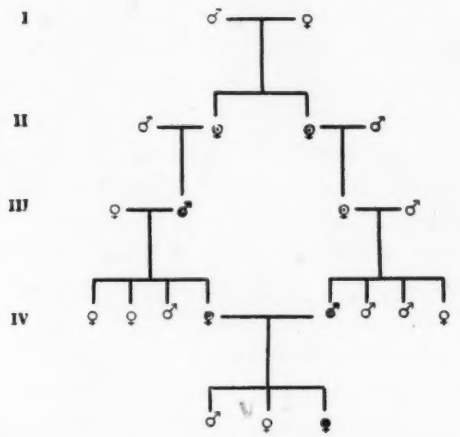

Fig. 27.—Pedigree in total color deficiency. Manifestation of the deficiency owing to consanguinity of the parents. The black circle indicates a person with color deficiency; the white circle with the black dot, a person who transmits the deficiency and the white circle, a normal person. (After Vogt and Franceschetti, in Schieck, F., and Brückner, A.: Kurzes Handbuch der Ophthalmologie, Berlin, Julius Springer, 1930, vol. 1.)

Fig. 28.—A boy who is totally color blind, with characteristic photophobia.

dark-adapted eye has also a reduced visual acuity and a relative central scotoma. Nystagmus is due to the loss of central fixation. The fact that the person is dazzled is easy to understand, because the apparatus of light adaptation either is absent or does not function.

Development of Color Sense.—A few words may be said about the hypothesis concerning the phylogenetic development of color sense.

Schrödinger [58] suggested that monochromatic vision was, phylogenetically, the oldest form; in such vision only different degrees of brightness, and no color, can be distinguished. Schrödinger expressed the opinion that in earlier periods of the earth's history the misty condition of the atmosphere due to its saturation with moisture allowed the light to reach the surface of the earth only in small quantities. Therefore, the color sense was undeveloped.

The faculty of distinguishing between yellow and blue is mostly considered to be a phylogenetically older faculty than that of the recognition of green and red. With regard to the heredity of color sense deficiencies, this opinion seems probably to be correct. Perhaps there may be a form of mutation. But to establish definite hypotheses, such as that of Ladd-Franklin and Lemmon [59] (who suggested that the red-green sense was developed by splitting off the elements corresponding to the yellow sensation), seems to me hardly permissible with present day knowledge.

PHENOMENA OF LOCAL ADAPTATION

I have hitherto dealt only with the color sense of the central part of the retina, of the macula or fovea. In the peripheral portions of the retina the color vision diminishes in proportion to the increasing eccentricity of the stimulated spot in the retina. The handbooks always repeat the statement that all colors can be perceived up to about 20 degrees and that there follow a zone which is red blind and then a red-green blind zone, total color blindness being assumed at the extreme periphery.

This opinion is generally accepted, but it is not correct. That color blindness of the peripheral parts of the retina is only relative was demonstrated by Tschermak,[60] a pupil of Hering, about forty years ago. If the stimulus is intense enough, namely, of sufficient objective saturation and extent, one is able to perceive all colors even at the extreme periphery of the field of vision.

If a piece of well saturated green or red paper about 10 cm. in diameter is placed in the extreme periphery of the visual field, one sees

59. Lemmon, V. A.: A Modification of the Ladd-Franklin Theory of Colour Vision, Am. J. Physiol. Optics **6**:449, 1925.

60. Tschermak, A.: Beobachtungen über die relative Farbenblindheit im indirekten Sehen, Arch. f. d. ges. Physiol. **82**:559, 1900.

the color without difficulty. But if the eye does not move, the color becomes invisible after a short time and only an uncolored sensation remains. Therefore, one may conclude that the stimulation of the same area for a short time causes color blindness from exhaustion. In comparison with the macula the periphery of the retina becomes fatigued more quickly.

This experiment is a remarkable illustration of the fact that the psychic correlative, the saturation, is determined not only by the specific type of the physical stimulus acting on the peripheral organ but by the condition of the body, and that changes in this are of the greatest importance.

PHENOMENA OF REVULSIVE LOCAL ADAPTATION

I shall now discuss the phenomena of revulsion—*"die Umstimmungserscheinungen,"* as Hering called them. These phenomena of the change in the response to stimulus are still often looked on as accidental occurrences or as curiosities. Hering studied the phenomena of adaptation by intensive investigations about sixty years ago, and his results are still valid. The chief suggestion is that the visual organ changes more or less rapidly under the influence of each successive illumination, whether the area is small or large. The change in response to stimulus is not confined to the zone directly affected by the light but extends to the whole retina, though in decreasing degree as the distance from the directly stimulated spot increases.

These phenomena are also called local adaptation, because they are caused by stimulation of a limited zone of the retina only, in contrast to general adaptation, for instance that of dark and light adaptation, which concerns the whole visual apparatus.

If one stares at a black spot for twenty seconds and then looks at a white field, one sees a very bright white spot on the latter. The white light does not produce the same effect in that part of the retina previously less affected when one was looking at the black spot. The same experiment can be carried out with a red spot, when a green after-image, as this phenomenon is called, will be perceived, or with a yellow spot, which produces a blue after-image.

In these experiments the change in response is studied in the zone of the retina which was previously affected by light. In other experiments is seen the alteration of excitability, depending on the environment of the part stimulated or on the differences of two neighboring fields. For instance, on looking at figure 29 one has the impression that the two gray V's are not of the same luminosity. When the surrounding black and white fields are covered, one sees that the gray lines are of the same brightness. They change only by reason of the quality of the two adjacent fields.

If after an exact fixation for about a minute the after-image is studied, it is perceived that its brightness completely accords with the inverse brightness of the original image. This fact demonstrates the validity of the phenomena called simultaneous and successive contrast.

If one looks at figure 30, fixing the eye exactly on the center of the white square for one or two minutes, another phenomenon will be observed: The immediately surrounding black becomes brighter, while

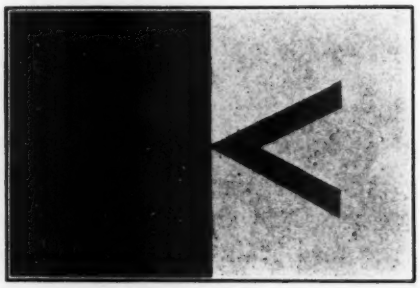

Fig. 29.—The two "V"s are of the same brightness on both sides. That on the dark background, however, appears by contrast to be lighter than that on the light background. (After Hering.[5])

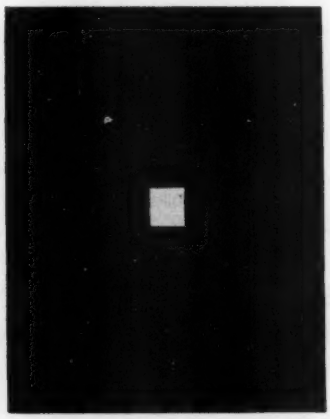

Fig. 30.—Demonstration of spatial induction of same color.

the white spot itself becomes more or less dark. That is a spatial induction in the same color *(gleichsinnige Induktion)*, which is the inverse of the antagonistic contrast already demonstrated. One may say that the antagonistic induction overcomes the simultaneous contrast; later the induction of the same sense predominates, which passes over into the successive contrast and the negative after-images.

These experiments show the extremely manifold reactions and the alternating effects in the visual substance. These are continually changing under the influence of stimulation by light and of regeneration taking place within the visual substance.

One may object that the alterations shown by these experiments are effected by an extreme degree of fatigue, such as does not normally influence the eye. But careful observation proves that the same effects arise, though in less degree, by short exposure. The contrast phenomenon is noticed even with momentary exposures.

Black Sensation.—The facts just reported are of importance in clearing up the question of the black sensation. The physicist maintains that black is seen when objectively there is no stimulus. A thing seems black when all light falling on it is absorbed and not reflected. That is the definition of a black body. But it accords only with the physical circumstances, not with the physiologic or the psychologic.

When one is in an absolutely dark room, the visual sensation is not a deep black but a more or less dark gray. When one awakes before dawn, all objects in the room look grayish. As the illumination increases, the difference in the brightness of the objects becomes more and more noticeable, some becoming brighter and others darker, until one perceives a real black. This sensation is called forth by contrast or simultaneous induction. This can be demonstrated by taking a gray paper with a hole 1 cm. in diameter in the center and observing through it an evenly illuminated gray paper placed below it. When the paper with the hole in it is moved toward and then away from the window, the color of the paper observed through the hole will appear to change from gray to black.

This experiment demonstrates, as was first shown by Hering,[15] that the black sensation arises only in an indirect manner in the visual substance. The opinion that black is not a sensation because there is no stimulus corresponding to it was adopted by von Kries [61] and later by Kirschmann.[62] But an ordinary man is certainly convinced that black is a sensation just as much as white or a color.

The same applies to brown as to black. Only a blackish orange can be perceived if the surroundings are illuminated and the intensity of the orange is not too strong. To prove this one can use the same gray paper with the hole 1 cm. in diameter that was just mentioned, with an orange paper placed below it.

Importance of Contrast.—The importance of contrast for distinct vision is great. Only by contrast can individual objects be distinguished sharply from one another. Reading also is possible only through contrast.

In consequence of the diffusion of light in the eye caused by irregularities in the media, the image thrown on the retina is not sharp. Therefore, there can be no exact vision. Figure 31 shows the suggested

61. von Kries,[8] p. 8.

62. Kirschmann, A.: Farbenterminologie, Neue psychol. Studien **2**:127, 1926.

course of the distribution of the light on the retina effected by two bright objects with dark surroundings. The height of the ordinates representing the luminosity on the different parts of the retina does not change suddenly, corresponding to the limit of the white field. The psychic effect would be a very faded image.

Simultaneous contrast by its alternating effect (*Wechselwirkung*) depresses the lower part of the curve and raises the other. In this manner, psychically, a sharp boundary is again produced. Figure 32, published by Tschermak,[63] suggests a possible explanation of this complicated matter.

The biologic significance of local adaptation or induction is founded on the fact that in the immediate neighborhood of a stimulated zone in the retina the excitability for this form of stimulus is increased.

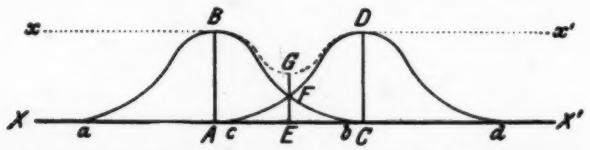

Fig. 31.—*aBb*, and *cDd* represent the diffuse effect of light on the retina by two adjacent luminous objects (points). The distribution of the intensity of light is indicated by the dotted line *xGx'*. (After F. B. Hofmann.[3])

Because small movements of the eyes are constantly occurring, even when the gaze is fixed on a point, and because there is still more movement when the eyes are moved, the increased excitability causes a high degree of sensation. It brings about a constancy of sensation which would rapidly change or vanish if an object was looked at fixedly. That this regulative function does not overcome extreme degrees of fatigue may be observed by fixing the gaze on slightly grayish spots on a white paper for two or three minutes; the spots will disappear completely.

A series of observations seems to prove that the function of contrast depends in some degree on general light or dark adaptation, which I shall speak about later.

The observation that in the morning with increasing illumination the contrast between the color of different objects becomes more distinct leads to the conclusion that the dark-adapted eye is less able to produce the phenomenon of contrast than the light-adapted eye. Certainly, that is to a great extent the reason why the dark-adapted eye has a low visual acuity—not more than about one sixtieth of that of the light-adapted eye. It is usually considered that visual acuity is dependent on the anatomic structure alone; but that is too simple an

63. Tschermak, A.: Ueber Kontrast und Irradiation, Ergebn. d. Physiol. **2**:726, 1903.

explanation. It does not take into consideration, for instance, the constant small movements of the eye which are present even when an attempt at exact fixation is made. Nevertheless, it cannot be denied that the anatomic structure is the foundation on which visual acuity is based.

But if this is imputed solely to the anatomic structure of the retina, the explanation seems to be insufficient. Although the fovea centralis has only cones and no rods, and although the rods are probably the sole

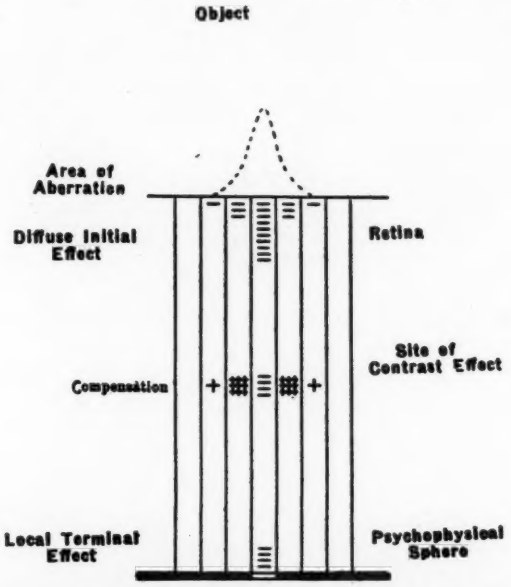

Fig. 32.—Scheme to illustrate formation of contrast in central parts of the retina. A diffuse initial effect is produced in the retina, corresponding to the aberration of light, in conformity with the punctiform object. By contrast effect, in more central parts of the visual pathway the parts of the object which correspond to the less illuminated points of the retina are obscured (indicated by cross hatching). At the same time the place of maximal exposure to light (corresponding to the height of the dotted line) is also reduced in its exciting effect by its surroundings, which are less illuminated. As final effect there arises in the psychophysical sphere a sharp though less bright image, corresponding to the object. (After Tschermak.[68])

apparatus which functions in the fully dark-adapted eye, the light-adapted eye has near the fovea a visual acuity of about one fifth. The apparatus for dark vision or scotopia has therefore, for some reason, a lower value for visual acuity. Foremost of all, I think that here the phenomena of contrast must be taken into consideration, because the other phenomena of local adaptation are diminished in comparison with the light-adapted eye, e. g., the ability to produce negative after-images.

If with the dark-adapted eye one gazes at a white field with low illumination for two or three minutes, one perceives hardly any afterimage.[64]

On the other hand, a high degree of light adaptation also is not suitable for the manifestation of contrast. As a result, the visual acuity decreases when the general illumination increases, and the resulting light adaptation of the eye exceeds a definite degree. Figure 33, published by Hecht, shows that central visual acuity is dependent on the degree of general illumination. In greater degrees of illumination the function increases to a certain point but finally decreases when the illumination begins to dazzle the eyes. An evidence of damage by light is the red vision, or erythropsia, which is produced in an extreme degree by dazzle from sunlight reflected by snow. However, to deal fully with this interesting question would take me too far from the subject.

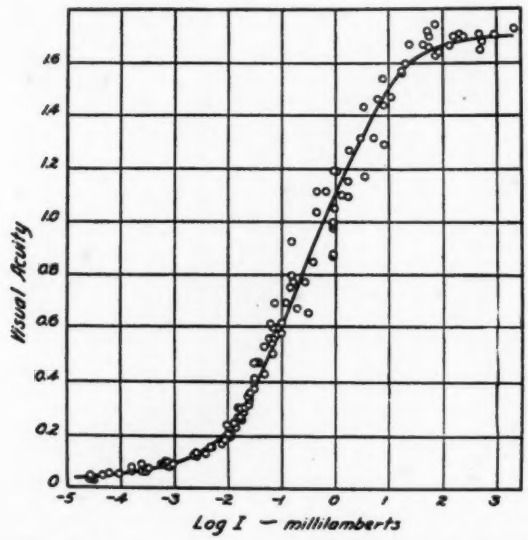

Fig. 33.—Relation between visual acuity and illumination. The original intensities have been multiplied by 0.072 to convert them into millilamberts. (After Hecht, S.: Visual Acuity and Illumination, Arch. Ophth. **57**:564, 1928.)

LOCAL DIFFERENCES IN ADAPTATION

I have already mentioned the phenomena of change in excitability which are less pronounced in the fovea than in the periphery of the retina. This may be due to the fact that the macula lutea is doubly

64. Brückner, A.: Untersuchungen zur Dunkeladaptation des menschlichen Auges, reprinted from the report of a joint discussion on vision, Physical and Optical Societies, London, June 1932.

represented in the visual cortex of the brain. The anatomic proof of this was elucidated by Arved Pfeifer.[65] He demonstrated that in the posterior part of the corpus callosum the nerve fibers corresponding to the macula divide and cross from one side to the other. The number of neural elements excited by a stimulus is therefore larger and the sum of the chemical processes greater in degree. Moreover, the sum total of the fibers corresponding to the macula of each eye comprises much more than half of all the fibers for one eye. This proves that the "weight" of the sensation in the sense of the quantity of the underlying process (Hering) is much greater when the macula is stimulated than when a peripheral area is involved. Certainly this favors central vision by producing greater constancy of sensation.

On the other hand, the pronounced local adaptation of the retinal periphery is of no less importance. Some authors attribute to the retinal periphery a special sense for the perception of movement. It is indeed remarkable how acute is perception of small movements, e. g., that of a fly as seen by indirect vision. Biologically this function is of importance because by it one easily recognizes any danger coming from either side or from above. This so-called sense of movement is not a specific one, but is due to quick local adaptation, which enables one to perceive the small differences of brightness dependent on changes in the position of objects.

It would also be of interest to explain the phenomena of contrast from another point of view. According to Hecht's application of the all or nothing law to the eye, each element in the retina has its own threshold; with the increase of light still further elements are stimulated. In the peripheral portion of the retina of the light-adapted and in the slightly dark-adapted eye (therefore in moderate illumination) the number of stimulated elements is relatively small, and therefore, in accordance with this supposition, the intensity of the chemical (or physical) processes induced must generally be smaller than in the completely light-adapted eye in higher illumination. Apparently in the first instance the visual substance must be sooner exhausted or changed in regard to its response to stimulus, which is in accordance with the phenomena of local adaptation.

Measurement of Phenomena of Local Adaptation.—All the facts mentioned prove the necessity for an exact measurement of the phenomena of local adaptation, especially that of contrast. This task is very difficult, because through the influence of an illuminated field an increasing change is constantly effected; even though contrast develops

65. Pfeifer, R. A.: Myelogenetisch-anatomische Untersuchungen über den zentralen Abschnitt der Sehleitung, in Foerster, O., and Wilmanns, K.: Monographien aus dem Gesamtgebiet der Neurologie und Phychiatrie, Berlin, Julius Springer, 1924, no. 43.

momentarily, it increases with the duration of the stimulus. Therefore, not only the difference between the two contrasting fields and their size is decisive, but also the duration of the influence. Some experiments concerning the quantitative measurement of contrast have been carried out by Pretori and Sachs [66] and some psychologists, but the results seem to be insufficient to allow the deduction of laws therefrom.

Difficulty of exact measurement of the phenomena of local adaptation is the reason that there is insufficient information concerning individual differences of adaptation. The anomalous trichromats are affected in a higher degree by contrast. Therefore, gray spots beside red appear green to them—a phenomenon not seen by any one having normal color sense. Nevertheless, statements made by those with normal color vision show that even among them differences exist.

Individual differences in the development of contrast are perhaps founded on differences in the amount of the hereditary mass, and as a consequence in the amount of the chemical processes in the sensitive substance. The same suggestion holds good as for the differences of local adaptation in the central and peripheral zones of the retina.

PHENOMENON OF CONSTANCY

A further form of change of perception is the phenomenon of constancy, which Hering mentioned long ago. During the last twenty-five years it has been intensively studied by psychologists. Katz and Jaensch [67] and their pupils especially devoted a great deal of research to this subject.

A white paper of definite brightness in daylight will appear slightly but definitely darker when observed in shadow, but it will still appear to be white. When the brightness of the shaded white is measured, it is seen to be much less than it was in full illumination. With allowance for the illumination or, better, the shade, the sensation is heightened. Therefore, the white paper seems brighter and, allowing for the luminosity, nearer to the sensation perceived when the paper was illuminated by ordinary daylight. The phenomenon is called transformation, because the color is transformed, nearly to the sensation called forth by ordinary conditions.

The change in color produced in this manner is also called albedo color, because albedo signifies the relation of the quantities of light

66. Pretori and Sachs: Messende Untersuchungen des farbigen Simultankontrastes, Arch. f. d. ges. Physiol. **60**:71, 1895.

67. See the short abstract by A. Gelb: Die Farbenkonstanz der Sehdinge, in Bethe, A., and others: Handbuch der normalen und pathologischen Physiologie, Berlin, Julius Springer, 1929, vol. 12, pt. 2, p. 524.

falling on and reflected from a surface. One is said to perceive this physical relation by the phenomenon of constancy.

This phenomenon is always convincing when demonstrated in non-colored illumination or shadow. But it is also seen when the illumination consists of colored light, when one can often perceive the specific colors of the objects, namely the colors perceived in white illumination such as daylight.

These illustrations show how these phenomena of constancy, etc., help in the better orientation of man in his environment in that they stabilize it by producing a constancy of sensation. In this way one recognizes objects more easily than if they called forth different sensations. Naturally, it is necessary to realize the differences of illumination and take them into consideration, although this allowance is not fully conscious. If this were not done, there would be many errors of judgment.

A similar phenomenon of transformation is observed in spatial judgment. In judging the size of an object at a distance, e. g., a man, one takes into account both the distance and the known size of a man and does not regard him as being as small as if his known size were not taken into account.

The position of an object may also be considered. For instance, a piece of wire when held toward one in an inclined position seems to be nearly as long as in a vertical position when one is able to recognize its position. Some observations concerning these facts have been communicated by Gellhorn.[68]

All these examples demonstrate how one is able to recognize the same object under different physical or physiologic conditions which should produce different sensations and to acknowledge it as the same object by physiologic or psychologic conversion.

SEAT OF LOCAL ADAPTATION

The question now arises: Where are these processes localized in the visual tract?

The phenomena of constancy or transformation must be bound to higher psychic functions, which are ordinarily called judgments in a larger sense. Here doubt seems to be excluded.

Helmholtz [69] considered that the genuine contrast phenomena were based on a kind of judgment, but he did not exactly define what he meant by this. But it is difficult to understand how such strictly regulated phenomena can be subject to judgment, since they are also perceived by persons who have no idea of the laws governing them. Therefore,

68. Gellhorn, S.: Beiträge zur Physiologie des optischen Raumsinnes: II. Ueber die Beziehungen zwischen physiologischer und mathematischer Perspektive, Arch. f. d. ges. Physiol. **208**:361, 1925.

69. Helmholtz,[18] p. 250.

one must consider local adaptation as a process physiologically determined.

Hering, although he never expressly said so, probably suggested that the local adaptation was localized in the retina. Other authors localized the processes of contrast in the layer of amacrine cells of the retina, because their dendrites provide a connection between neighboring parts of the retina. But there are observations which seem to prove clearly that the phenomena in question are not carried out in the retina alone.

Some writers have noticed that it is possible under certain conditions to see in the monocular field the blindspot, which is itself devoid of sensation. Even in binocular vision some observers are able to see both blindspots. This visibility of the blindspot has been the subject of repeated research. At first the blindspot appears as a dark, well defined disk, often surrounded by a small bright corona, corresponding to sensitive parts of the retina. When colored illumination is used, the blindspot appears in the contrast color. It can also be perceived as a negative white or colored after-image, depending on the nature of the preillumination. In order to facilitate the task it is helpful to make use of a vertical line between a white and a black field falling exactly across the area of the visual field corresponding to the blindspot, as seen in figures 34 and 35.[70a]

Since in the peripheral organ there is no light-sensitive element corresponding to the blindspot, the fundamental processes producing visibility of the blindspot must lie in a more central part of the optic pathway. Such an induction between adjacent parts seems possible only between nerve cells, not between fibers, and it must be supposed to be situated either in the corpus geniculatum externum or in the visual cortex in the posterior lobe of the brain.

The opportunity to examine 2 men injured in the war enabled me to make some instructive observations concerning this question.[71]

A German officer was wounded by a fragment of a shell which severed the optic pathway immediately above the corpus geniculatum externum and produced homonymous hemianopia and other nervous deficiencies. It was possible by illuminating the seeing half of the visual field to produce a sensation in the contrast color in the blind half. If the illumination was white, the blind half appeared black; with colored illumination, for instance blue, the blind half appeared yellow. Negative after-images were produced in this manner according to the well

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70. (*a*) Brückner, A.: Ueber die Sichtbarkeit des blinden Fleckes, Arch. f. d. ges. Physiol. **136**:610, 1910. (*b*) Tschermak, A.: Ueber Merklichkeit und Unmerklichkeit des blinden Fleckes, Ergebn. d. Physiol. **24**:330, 1925.

71. Brückner, A.: Zur Frage der Lokalisation des Kontrastes und verwandter Erscheinungen in der Sehsinnsubstanz, Ztschr. f. Augenh. **38**:1, 1917.

known laws. This observation proves that in this case the phenomenon of local adaptation was localized not in the corpus geniculatum externum but probably in the visual cortex of the posterior lobe of the brain.

The second case was that of a young soldier wounded in the back of the head in the visual region. He had a defect in the visual field

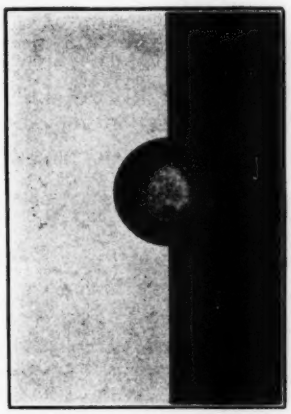

Fig. 34.—Appearance of the blindspot of the left eye when it falls on the boundary between white and black. The center of the blindspot is brightened by contrast. (After Brückner.[70a])

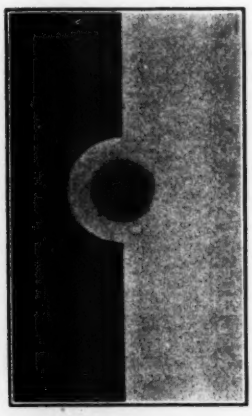

Fig. 35.—Appearance of the blindspot of the left eye on the boundary between black and white. The blindspot appears bright; the center appears darker by contrast. In the periphery of the blindspot there are slight appearances of simultaneous contrast within the seeing retina. (After Brückner.[70a])

of both eyes, the nature and form of which can be seen in the figure 36. It was possible to produce contrast colors in the blind area as in the first case. About the particular point of these observations there is no need to speak. This observation shows that the phenomena of contrast

seem to be localized in centers lying still higher than the visual cortex, that is to say, in transcortical centers.

Of some interest is the fact that both cases demonstrate a reciprocal influence of both hemispheres, because in the hemianopia in the first case and according to the form of the scotoma in the second case both hemispheres must be affected directly or indirectly by contrast. These cases suggest that perhaps there is a transcortical center which fuses the impressions of both visual spheres.

This suggestion falls into line with phenomena of binocular contrast: When one eye is stimulated by a colored field, the other eye sees the contrast color in the corresponding surrounding zone, although not in so distinct a manner as in monocular contrast.

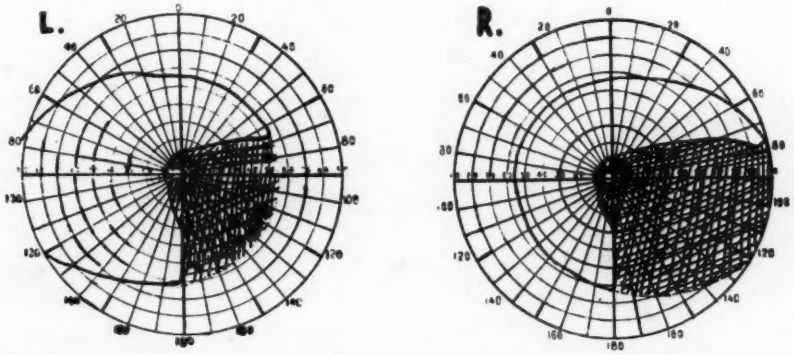

Fig. 36.—Defect in visual field of a wounded soldier. (After Brückner.[71])

Nevertheless, it seems to me that the centers of the physiologic processes on which the phenomena of local adaptation and contrast are localized are probably situated in all stations in the visual pathway. As Jaensch has suggested, the different stations probably influence each other.

All this shows that nature strives to unite the whole visual system and to guarantee thereby the constancy of visual reception.

With respect to the question of the localization of the phenomena of local adaptation some recent investigations are of interest, especially those dealing with the change of the electric behavior under the influence of light. They show a constant current which in the eye of the vertebrate is directed in the outer part of the circuit from the cornea to the posterior pole of the eye. This co-called duration current is subject to characteristic changes when the eye is illuminated.

Recently so-called electroretinograms of the human eye have been made by Sachs.[72] Figure 37 demonstrates some of his observations.[73]

72. Sachs, E.: Die Aktionsströme des menschlichen Auges, ihre Beziehung zu Reiz und Empfindung, Klin. Wchnschr. **8**:136, 1929.

73. Kohlrausch,[23] p. 149.

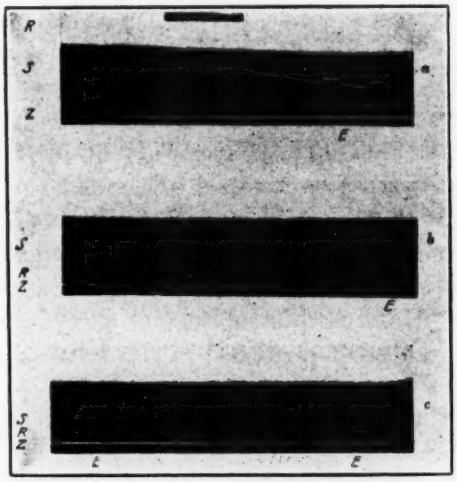

Fig. 37.—Electroretinogram of a man: adaptation state and secondary elevation on red stimulation and blue stimulation; specific color effect? *a*, dark adaptation, red, 2 lux, 10° visual field, fixed centrally; *b*, light adaptation, red, 5 lux, 10° visual field, fixed 14° peripherally; *c*, dark adaptation, blue, 1 lux, 10° visual field, fixed centrally. *R* indicates photographic or electromagnetic marking of stimulus; *S*, string; *Z*, time in one-fifth second intervals; *E*, gaging with 0.1 millivolt, by string, electrodes and eye. (Original curves after E. Sachs,[72] reduced to one third of the original size.)

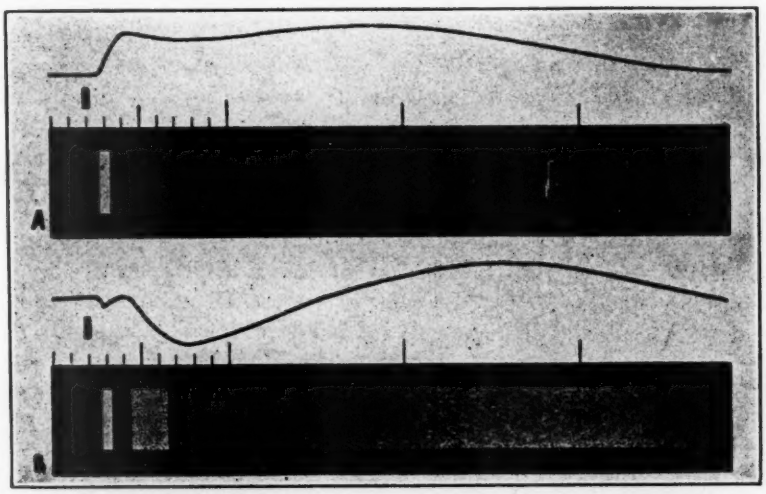

Fig. 38.—Parallelism between the retinal currents of the hematothermal species and the periodic visual sensations of man: *A*, momentary illumination with red of very long waves; *B*, with blue. Corresponding retinal current and visual sensation are shown one above the other, since the actual time interval is not accurately known. Time in seconds; the first second divided in tenths. (After Kohlrausch.[28])

Red light produces in the dark-adapted eye a slight oscillation, which is in accordance with the feeble stimulating value of red light on the dark apparatus of the eye. In the light-adapted eye the curve runs in another direction. Illumination with blue light on the dark-adapted eye caused a remarkable oscillation, in accordance with the brightness of the sensation from blue light in the eye. These results agree with those obtained from experiments on the eyes of animals.

As another type of the action current corresponding to the periodic course of the after-image I show figure 38, published by Kohlrausch.[73]

Probably the quantitative differentiation of the stimulating processes is already effected in the peripheral organ. In the continuation of the optic pathway the different processes in the retina are represented by different frequencies of the electric current, as shown by Adrian and Kohlrausch. The different color sensations run parallel to those in the central organ. This opinion was expressed by Fröhlich.[74]

When it is remembered that electric phenomena are perhaps only accompaniments of exciting chemical processes of an antagonistic character, the explanation of local adaptation, given before, becomes still more evident. All parts or stations of the optic pathway interfere with this phenomenon.

74. Fröhlich, F. W.: Die Empfindungszeit, Jena, Gustav Fischer, 1929.

(To Be Concluded)

CONGENITAL BUPHTHALMOS

COMPLICATED BY DISLOCATION OF LENS AND HEMORRHAGE INTO VITREOUS WITH COMPLETE RECOVERY OF CENTRAL VISION

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The following case is reported because of the favorable result that followed a severe injury and a stormy course in the only buphthalmic eye of a patient:

History.—D. L., a white man aged 31, of Italian extraction, entered the ophthalmologic service of the Cook County Hospital on April 4, 1936. He gave a history of having been struck in the right eye by a finger fifteen hours previously. After the injury he became totally blind in his right eye.

When the patient entered grammar school it was found that both of his eyes were larger than normal and that he had no vision in his left eye. The diagnosis was said to be bilateral congenital glaucoma. In 1911 a Lagrange type of operation was performed at the usual location on the right eye by Dr. Ben Witt Key, of New York. After this, the patient regained sufficient vision to finish the grades. He wore glasses for seven years after the operation, but discarded them in 1918. In 1933, owing to repeated attacks of severe pain, the left eye was enucleated. Until the recent injury, he was able to read the newspapers and see motion pictures. His general health had always been good, and there was no history of ocular disease in his family.

Ophthalmologic Examination.—Vision in the right eye was limited to perception of light with faulty projection. Vision in the left eye was nil (a prosthesis was worn).

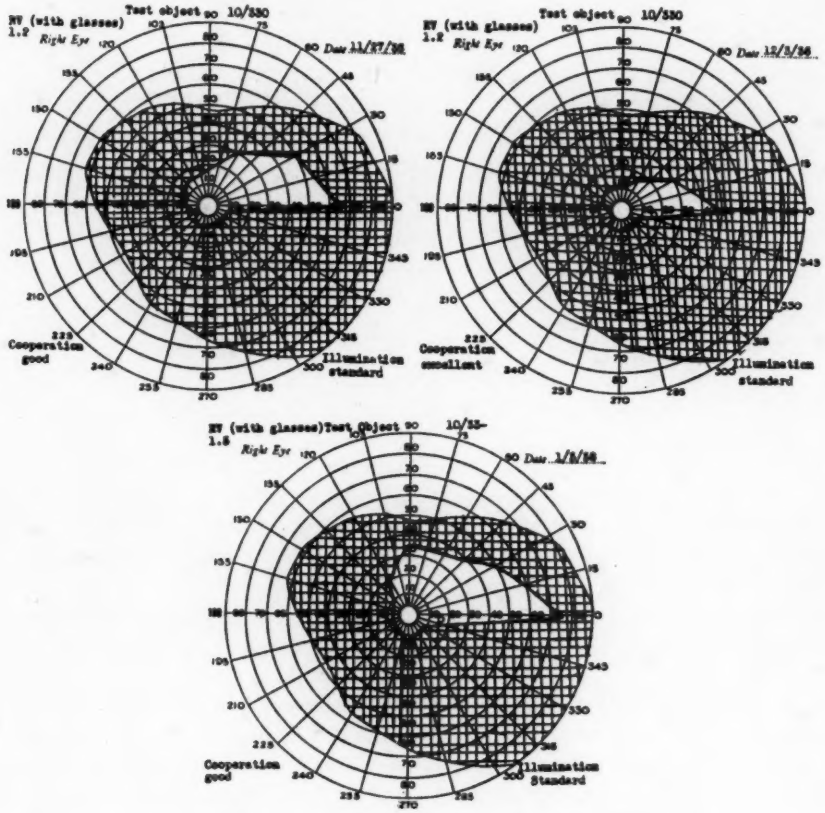
Both lids of the right eye were markedly ecchymotic. The external ocular movements were normal. Recent subconjunctival hemorrhages were present on the nasal and inferior quadrants of the bulb. The sclera was uniformly distended and appeared bluish. The cornea appeared globular and measured 17 mm. in the transverse diameter. No ulcerations or opacities were seen on its surface. The anterior chamber was filled with blood. A red fundus reflex could not be elicited. The tactile tension was normal.

The stump of the left eye was smooth and even and appeared somewhat retracted. The conjunctival cul-de-sac was narrowed; only limited movements of the prosthesis were present.

Physical Examination.—The patient was well developed and well nourished and did not appear acutely ill. The skin presented diffusely scattered patches of vitiligo. The nose and ears were normal. The teeth showed evidence of decay in the region of the upper right and lower left molars. The tonsils were enlarged, and cheesy material exuded from their crypts on pressure on the pillars. The thyroid gland was not palpable, and no glands or masses were felt in the neck. The blood pressure was 126 systolic and 84 diastolic. The heart, lungs, abdomen and extremities were normal.

Laboratory Examination.—The urine, the blood count, the blood chemistry, the bleeding time and the coagulation time were normal. Intradermal tuberculin tests gave negative results. The basal metabolic rate was —6. Roentgenograms of the chest and skull revealed no abnormal changes.

Diagnosis.—The condition was diagnosed as: (1) traumatic intraocular hemorrhage involving the right anterior chamber and possibly the deeper structures of the right eye and (2) congenital buphthalmos.



Visual field of patient taken on three different dates.

Treatment and Course.—The patient was put at absolute rest in bed. Hot applications and an ointment containing 1 per cent atropine sulfate were applied three times daily to the right eye. Four weeks later, with the foregoing regimen, the external swelling and redness had largely abated. The subconjunctival swelling and hemorrhages had disappeared. The anterior chamber appeared deep and was free from blood. The iris was tremulous, dull and lusterless. A coloboma of the pupil was present between 11 and 1 o'clock. A dark black mass was seen occupying the pupillary area. The tactile tension remained normal.

On June 2 a red fundus reflex was first obtained, and the vision had improved to ability to count fingers at 2 feet (60 cm.). The tension was 14 mm. of mercury (Schiötz).

On June 17 the vitreous had cleared sufficiently to permit a hazy view of the disk and the retinal vessels. A mass of grayish white tissue about 2 by 5 by 8 mm. was noted in the vitreous. This mass was firmly adherent to the ciliary body at a point about 2 mm. in front of the ora serrata at 3 o'clock. From this point of attachment the mass was observed moving backward and forward in harmony with movements of the eye, alternately obscuring and clearing the pupillary space.

On October 26, with a + 10.00 sphere combined with a + 2.00 cylinder, axis 5, the vision in the right eye had improved to 1.2-3. Studies of the peripheral visual field revealed an almost complete loss of the nasal field associated with a marked defect in the inferior temporal quadrant. A faint circumciliary flush was present. The white mass in the vitreous remained unchanged. The optic disk and retinal vessels were clearly visible. The nerve head appeared pale. The vessels of the disk were pushed nasalward, and a slight glaucomatous excavation was present. The tension was 18 mm. of mercury (Schiötz). Three carious teeth were extracted and the daily administration of atropine sulfate was discontinued.

On November 17 the patient complained of pain in his right eye. The eyeball felt hard to touch and still appeared irritated. The tension was 28 mm. of mercury (Schiötz). The visual fields exhibited a further concentric contraction in all meridians. A mixture of 2 per cent pilocarpine hydrochloride and 0.5 per cent physostigmine salicylate administered three times daily brought about only a temporary reduction in tension. On withdrawal of the miotic, an immediate rise to 38 and 45 mm. of mercury followed. Epinephrine packs (1 : 1,000) under the upper lid had only a temporary effect in lowering the tension.

On Jan. 27, 1937, tonsillectomy was performed. After this operation the patient's general physical condition improved greatly and he gained 12 pounds (5.4 Kg.) of weight within the next four weeks.

On February 17 a + 10.50 sphere combined with a + 4.00 cylinder, axis 180 (for near vision, addition of a + 3.50 sphere), improved the vision of the right eye to 1.5 with ability to read Jaeger test type 1 at 13 inches (33 cm.). The tonometric readings had dropped to 13 mm. of mercury and remained within normal limits since then without the use of miotics. The patient was discharged.

He was not seen again until Jan. 2, 1938. At that time the vision in his right eye with glasses was 1.5 with ability to read Jaeger test type 1 at 13 inches. The tension was 13 mm. of mercury (Schiötz). The visual field had increased 10 degrees in the temporal and 15 degrees in the superior meridian. The globe was pale. The white mass in the vitreous appeared as described previously, but seemed thinner, resembling a veil. The retinal veins were dilated. The disk was pale, but showed only a slight glaucomatous excavation.

COMMENT

The buphthalmic eye, owing to its prominence and greatly thinned scleral coat, is more prone to injury than the normal eye. The suspensory ligament is overstretched. Rupture of the zonule leading to dislocation of the lens frequently follows even the slightest traumatism.

In the case reported, at the time of the injury a backward dislocation of the lens took place. This was obscured by the associated massive hemorrhage into the anterior chamber and the vitreous. The freely swinging white mass just back of the ciliary region, observed at a later date, was attached by part of the torn suspensory ligament and

undoubtedly contained shrunken remnants of lens material covered by connective tissue and exudate.

The transient rise of tension and the persistence of pericorneal irritation disappeared on improvement of the patient's general physical status and the elimination of all frank foci of infection. The drop in tension, however, might have occurred without tonsillectomy, as there were no signs of uveitis as a cause for the increase in intraocular pressure. The visual fields were characteristic of glaucoma. The entire nasal field and a sector-shaped defect in the inferior temporal field were lost. The optic nerve showed evidence of atrophy, with a slight excavation of the lamina cribrosa. These changes most likely anteceded the recent disturbance and were presumably present at the time the patient first presented himself for treatment.

The remarkable final central visual acuity, the maintenance of normal intraocular tension and the absence of any further constriction of the visual fields over a period of a year offer strong supportive evidence of the efficacy of an early and properly performed drainage operation in a case of congenital glaucoma.

106 Market Street.

CIRCULATION OF THE AQUEOUS

VII. A MECHANISM OF SECRETION OF THE INTRAOCULAR FLUID

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AND
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In the course of an investigation on the mechanism of reabsorption of the intraocular fluid [1] it was found that the ciliary body shows an irreciprocal permeability to water, allowing fluid to pass with ease from the ciliary capillaries to the posterior chamber but obstructing the passage of fluid in the reverse direction. Phenomena of this type have been demonstrated in many other tissues.[2] Hitherto, however, no adequate physical explanation of such phenomena has been suggested. The present investigation was undertaken with the aim of discovering, if possible, the character and mechanism of the irreciprocal permeability of the ciliary body. In brief outline, it was first discovered that the ciliary body shows an irreciprocal permeability to certain dyestuffs as well as to water and that the behavior of the dyes indicates that an electrical phenomenon is involved. This led us to an investigation of the source of the energy required to perform the physical work involved in the irreciprocal permeability and finally to an analysis of the components of the mechanism by which this energy was transformed into physical work. In the end it was found that an adequate understanding of the mechanism of irreciprocal permeability to dyestuffs could account also for the irreciprocal permeability to water.

It will be seen that the investigation which we are reporting is a complex one involving several different types of experiments. In order to facilitate the continuity of the argument and to avoid confusion from

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From the Wilmer Ophthalmological Institute of the Johns Hopkins University and Hospital.

This investigation was supported in part by a grant from the John and Mary Markle Foundation.

1. Friedenwald, J. S., and Pierce, H. F.: Circulation of the Aqueous: II. Mechanism of Reabsorption of Fluid, Arch. Ophth. **8**:9 (July) 1932; Tr. Am. Ophth. Soc. **31**:143, 1933.

2. Gellhorn, E.: Das Permeabilitätsproblem: Seine physiologische und allgemein-pathologische Bedeutung, in Gildemeister and others: Monographien aus dem Gesamtgebiet der Physiologie der Pflanzen und der Tiere, Berlin, Julius Springer, 1929, vol. 16.

details of experimental technic, the experimental protocols appear in small type and the text in large type, the two portions being so arranged that they can be read continuously. A summary is inserted at the end of each section.

I. PERMEABILITY OF THE CILIARY BODY TO VARIOUS ACID AND BASIC DYES[3]

Most previous investigators[4] on the permeability of the blood-aqueous barrier have used as their criterion the appearance of the dye in the aqueous humor after intravascular injection. They have shown that most acid crystalloid dyes appear in the fluid while basic dyes do not. These investigations give no clue as to whether the dye has entered the ocular cavity by way of the ciliary body or through some other tissue, e. g., the iris. As long ago as 1882 Ehrlich[5] showed that fluorescein enters the anterior chamber by way of the iris, and subsequent studies by Hamburger[6] demonstrated that the contribution of the ciliary body to the intraocular diffusion of fluorescein was probably insignificant. We have studied the passage of dyes through the ciliary body directly, observing their movement in the direction from blood to aqueous and vice versa. The experiments were conducted as follows:[7]

To study the passage of dyes from the blood to the intraocular cavity, the dye (from 0.04 to 0.2 millimols per kilogram) was injected intravascularly into an albino rabbit. After the injection, the eye was enucleated with the animal under ether anesthesia; it was opened equatorially, and the vitreous and lens were removed with gentle pressure of the thumb of one hand while the inverted eyeball

3. The physical and chemical characteristics of the dyes used in all of the experiments reported in this paper are described in the Appendix.

4. Gaedertz, A., and Wittgenstein, A.: Arch. f. Ophth. **119**:395 and 403, 1927; **119**:755, 1928. Fischer, F. P.: Arch. f. Augenh. **100-101**:480, 1929.

5. Ehrlich, P.: Berl. klin. Wchnschr. **19**:388, 1882.

6. Hamburger, C.: Ueber die Ernährung des Auges, Leipzig, Georg Thieme, 1924.

7. In preliminary experiments attempts were made to use the frozen section technic. It was found that freezing the tissue caused a destruction or disturbance of its normal metabolism and led to erroneous and contradictory results with the dyes. On the other hand, if the living tissues were stained with the dyes the penetration of which was to be tested, and then fixed, the dye washed out of the tissue, especially from the epithelial layers. This led to an erroneous conclusion stated in a previous communication,[1] namely, that methylene blue injected into the vitreous does not stain the ciliary body, including the epithelium. Actually, most basic dyes, including methylene blue, injected into the vitreous stain the epithelium but not the stroma. Obviously, therefore, it was necessary to use and observe the dye directly on surviving tissue. It was found that such tissue kept in Ringer's solution could be used for from two to four hours after killing the animal or enucleating the eye. Temperature variations between 20 and 40 C. seemed to have little or no effect. Changes of short duration in the oxygen tension from 0 to 150 mm. of mercury did not affect the tissue irreversibly.

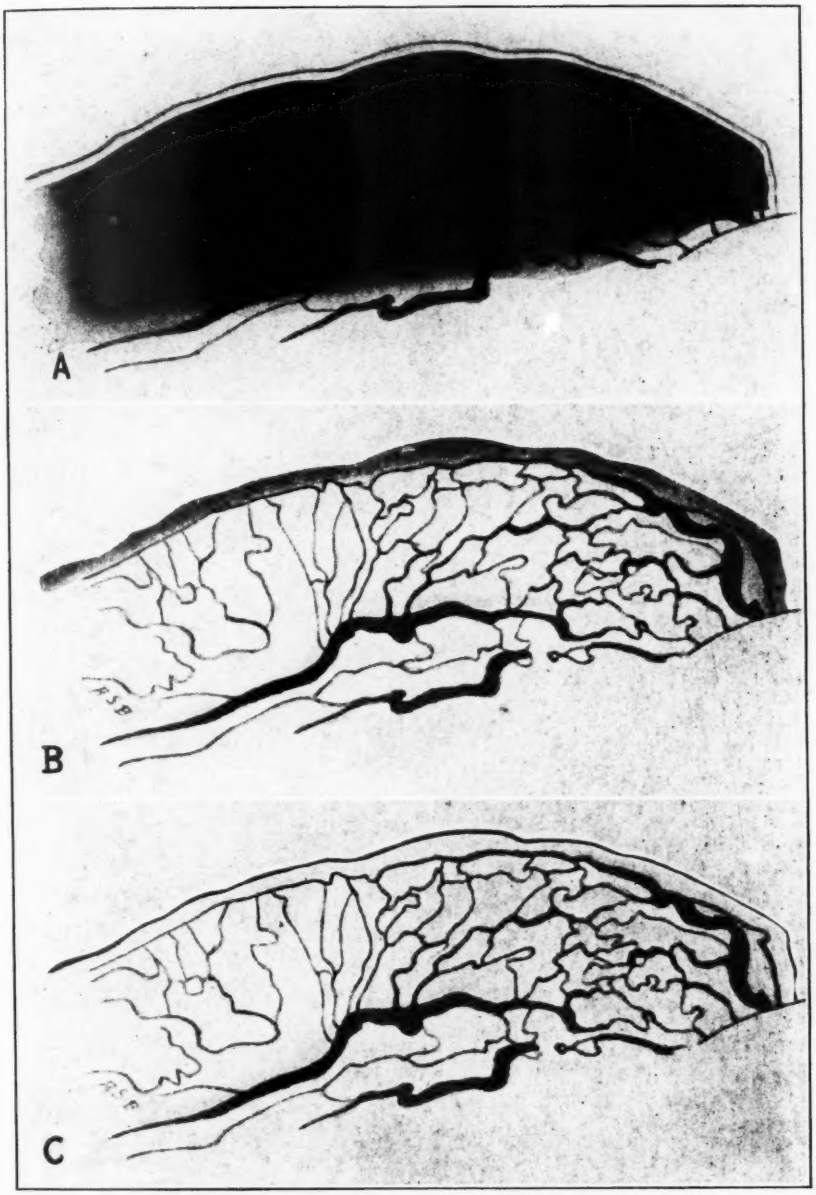

Fig. 1.—*A*, section of tissue showing the dye confined to the stroma. *B*, section of tissue showing the dye present in both the epithelium and the stroma. *C*, section of tissue showing the dye confined to the epithelium.

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was held between the thumb and the index finger of the other hand. The zonular fibers were examined for the presence of the dye. The iris and ciliary body were then removed in one piece with a tissue forceps and placed in a special Ringer's solution.[8] The ring of tissue was placed on a microscope slide with the ciliary processes upward and examined under a microscope (16 or 8 mm. objective).

When the dye fails to penetrate from the stroma to the epithelium the picture is produced that is shown in figure 1 *A*. The interpretation is sometimes difficult because the epithelium on the anterior tips of the ciliary processes may be so thin as to escape observation with the low power of the microscope. Certain acid dyes stain the epithelium feebly even when introduced through its free surface, and when penetrating from the stroma to the epithelium they may rapidly diffuse out of the latter tissue into the surrounding fluid, leaving the epithelium relatively colorless. The distinction between the picture under these circumstances and that shown in figure 1 *A* is that the margin of the stained area in the stroma is blurred instead of being sharp.. This difficulty was encountered particularly in the asphyxia and p_H experiments cited later.

To study the passage of dyes from the intraocular cavity to blood, the eye of an albino rabbit was removed and dissected in the manner previously described. The ring of tissue was cut into from ten to twenty sectors in a bath of Ringer's solution. These sectors were placed on slides (ciliary processes upward), and a ciliary process was lapped over the cut edge with the aid of a camel's hair brush (fig. 2). The excess fluid was drained off with blotting paper, and a minute drop (not more than 1 cu. mm.) of dye solution (approximately 0.001 molar) was placed on the moist surface of the glass next to the tissue. As soon as the vertical edge of epithelium was stained, the excess of dye was drained with blotting paper, and a few drops of Ringer's solution added. The tissue was observed under a microscope to determine the penetration of the dye.

One of the difficulties in determining whether or not the dye has penetrated arises from a spreading or creeping of the dye in the epithelium. This may happen either because the dye runs over the horizontal surface of the ciliary process in the moment of staining or as the result of slow diffusion of the dye from cell to cell after the staining solution has been removed. Two criteria are available to distinguish between such spreading of the stain and penetration, as illustrated in figure 1 *B*: 1. With critical focusing of the microscope, a sharp epithelium-stroma boundary, as in figure 1 *C*, is still to be recognized in case of nonpenetration.

8. The Ringer's solution referred to throughout this paper is that used by Dr. George O. Gey for tissue culture work. It contains per liter of solution: sodium chloride, 8 Gm.; potassium chloride, 0.37 Gm.; calcium chloride (anhydrous), 0.17 Gm.; magnesium chloride (anhydrous), 0.10 Gm.; disodium phosphate, 0.18 Gm.; sodium bicarbonate, 0.25 Gm.; carbon dioxide is added until the solution is completed. This solution was chosen after it had been found that experiments performed in an isotonic solution of sodium chloride gave erratic results. Tests were made to discover the effect of ions normally present in plasma. It was found that Ringer's solution, lacking only in calcium, caused the permeability of the membrane to increase, while 0.9 per cent sodium chloride plus a trace of calcium was adequate to maintain the normal permeability. The minimum amount of calcium required was found to be less than one-tenth that normally present in the body fluids. It is evident, therefore, that clinically possible variations in blood calcium cannot affect the membrane significantly. Further tests showed that even a considerable excess of magnesium could not be substituted for calcium.

2. The dye fades more rapidly in penetration than in creeping, since it diffuses into a larger volume in the former case than in the latter. In long-continued experiments dyes which fail to penetrate into the stroma are sometimes bleached out of the superficial layer of epithelium, leaving the second layer of epithelium holding most of the remaining dye. In general, basic dyes stain the tissues more intensely than acid dyes. This difference is not as marked at lower p_H.

Experiments were also performed in which the dye solution was injected directly into the stroma of the ciliary body either before or after enucleation. In other experiments the dye was injected directly into the vitreous. Identical results were obtained in regard to the penetration of dyes introduced either in vivo or supravitally.

Acid dyes (dyes which are anions in solution) introduced into the stroma of the ciliary body produce the picture illustrated in figure 1 *A*. The dye fills the stroma and does not penetrate into the epithelium. Acid

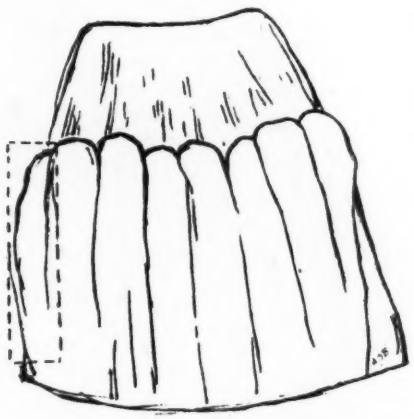

Fig. 2.—A segment of the iris and ciliary body viewed from behind. The overlapping ciliary process is indicated by the dotted lines.

dyes introduced into the epithelium produce the picture illustrated in figure 1 *B*. The dye penetrates into the stroma. If only a small amount of dye is used, the epithelium becomes colorless after a time, leaving a picture similar to that in figure 1 *A*. Basic dyes (dyes which are cations in solution) introduced into the epithelium fail to penetrate into the stroma, as illustrated in figure 1 *C*. Basic dyes introduced into the stroma penetrate rapidly into the epithelium, and if the concentration is not too high, the dye accumulates in the epithelium leaving the stroma relatively colorless, as in figure 1 *C*. Neutral dyes (dyes which are either uncharged or zwitterions in solution) penetrate with ease in both directions, as illustrated in figure 1 *B*.

The results with certain typical dyes which are not reduced by the tissue in air are summarized in table 1. The behavior of the other dyes which were used is reported in the Appendix. It can readily be seen

that the behavior of the dyes depends essentially on their ionic charge and not on their chemical structure. When similar experiments are performed on tissue asphyxiated either in an atmosphere of nitrogen or in the presence of 0.001 molar cyanide solution, it is found that the irreciprocal permeability to these dyestuffs disappears. Any particular dye now penetrates equally well from the epithelium to the stroma and from the stroma to the epithelium, and the phenomenon of accumulation disappears. However, a marked difference between the behavior of acid and basic dyes is to be noted, for now acid dyes penetrate rapidly and with ease, while basic dyes penetrate with great difficulty or not at all. This change in permeability produced by asphyxia was found in the case of nitrogen asphyxia to be reversible, the tissue regaining its normal

TABLE 1.—*Penetration of Dyes Through Stroma-Epithelium Barrier of Ciliary Body at Physiologic* p_H

Dye	Type	Penetration Normally		Penetration with Asphyxia	
		E to S	S to E	E to S	S to E
Crystal violet	Basic	0	++++	±	±
Malachite green	Basic	0	++++	±	±
Night blue	Basic	0	+++	0	0
Safranines	Basic	0	+++	0	0*
Eosin	Acid	+++	±	++	++
Bromphenol blue	Acid	+++	±	++	++
Rose bengal	Acid	+++	0	+	+
Rhodamine B	Neutral	++	++	++	++

0 indicates no penetration; ±, a trace of penetration; +, slow diffusion; ++, rapid diffusion; +++, slow accumulation beyond diffusion; ++++, rapid accumulation beyond diffusion; E, epithelium, and S, stroma.

* No penetration under cyanide; partially reduced under nitrogen.

characteristics when restored to air. Recovery from cyanide asphyxia has also been noted under certain conditions (see section III).

We have investigated in some detail the exact position of the barrier at which acid dyes are stopped from penetrating into the epithelium and basic dyes are stopped from penetrating into the stroma and have found that this barrier lies in the same region in each case, at the junction of the epithelium and the stroma. The penetration of basic dyes under asphyxia is blocked at the same place. Histologic study of this region reveals a forward continuation of Bruch's membrane which is visible in the flat posterior part of the ciliary body, becoming thinner and thinner as one follows it forward and being lost from view in the anterior portions of the ciliary body. We have not, however, been able to identify the stroma-epithelium barrier with this forward continuation of Bruch's membrane. Until more detailed knowledge is available, we shall refer to the barrier as the stroma-epithelium barrier. Further experiments on the nature of this barrier are reported here.

Summary.—There is a barrier between the stroma and the epithelium of the ciliary body which under asphyxia exhibits a selective permeability in favor of acid as against basic dyes. When the normal respiratory metabolism is operating, however, additional forces are active which facilitate the transfer of acid dyes from the epithelium to the stroma and of basic dyes from the stroma to the epithelium and impede the transfer of these dyes in the reverse direction. It is evident that these additional forces could be accounted for if there were in the ciliary body an ionic electric current carrying anions from the epithelium to the stroma and cations from the stroma to the epithelium. However, in order for an electric current to exist, there must be a source of energy and a carrier of electrons to complete the circuit. Since the phenomena the cause of which we are seeking to discover disappear under asphyxia, we have sought for the source of the energy in the respiratory metabolism of the tissue, which is the next step in our study.

II. OXIDATION-REDUCTION POTENTIALS OF THE CILIARY BODY

Since the behavior of dyes described and the assumptions of an electric current indicated that there must be a difference of free energy in the stroma-epithelium system, it was natural to look for this energy in the oxidative and reductive processes of the tissue. Clark and his co-workers [9] have shown that the intensity of oxidation-reduction activity of chemical systems that are capable of reversible oxidation may be measured in terms of electrical potential and that, in fact, chemical systems of this type, if properly connected by electrodes, are capable of generating an electric current. The potential of such systems may be measured directly electrically, but it may also be measured indirectly through the use of indicators which undergo a color change on oxidation or reduction. These investigators have prepared and studied a series of such indicators which may be used to determine the oxidation-reduction potential of systems by methods analogous to those by which p_H is determined through the use of p_H indicators. These studies refer to systems that are in thermodynamic equilibrium.

In the living tissues thermodynamic equilibrium does not exist. Instead there is a continuous interaction between many chemical systems. When these reactions proceed at constant rates, a steady state is established by a balance between the rates of oxidation and of reduction, which can be measured either potentiometrically or with oxidation-reduction indicators. The objections to the electrometric method need

9. Studies on Oxidation-Reduction: I-X, By the Staff of the Division of Chemistry, Hygienic Laboratory, United States Public Health Service, Hygienic Laboratory Bulletin 151, United States Public Health Service, 1928.

not be enumerated here.[10] The indicator method was used in the present study because of its directness and relative ease and because it enables one to determine the potential in all parts of the tissue at the same time. This involves some lack of precision, since the degree of bleaching of the various indicators can be estimated only roughly. Other sources of error with the indicator method are discussed by Cohen, Chambers and Reznikoff.[11] Nevertheless, given appropriate indicators, we believe that the potential of tissues can be determined with an error of less than ± 0.015 volt. The experiments were performed as follows:

TABLE 2.—*Oxidation-Reduction Potentials of the Ciliary Body*

		Reduction of Indicator					
	E'_0 at	Aerobic		Cyanide	Anoxia	Anaerobic	
Indicator	p_H 7.4 Volts	S	E	S	E	S	E
Binderschedler's green	+0.211	++++	++++	++++	++++	++++	++++
2,6,dichloroindophenol	+0.189	++++	++++	++++	++++	++++	++++
Toluylene blue	+0.101	++++	++	++++	++++	++++	++++
Lauth's violet	+0.050	++++	0	++++	++++	++++	++++
Cresyl blue	+0.034	++++	0	++++	++++	++++	++++
Methylene blue	−0.002	++++	0	++++	++++	++++	++++
Indigo trisulfonate	−0.099	+++	0	++++	++++	++++	++++
Indigo disulfonate	−0.143	+	0	++++	++++	++++	++++
Cresyl violet	−0.175?*	0	0	+++	+++	++++	++++
Dimethylphenosafranine	−0.275	0	0	0	0	+++	+++
Safranine T	−0.298	0	0	0	0	+	+
Estimated potential volts		−0.130	+0.100	−0.200	−0.200	−0.290	−0.290

0 indicates no reduction; +, one-third reduced; ++, one-half to two-thirds reduced; +++, one-third to nine-tenths reduced; ++++, over nine-tenths reduced; S, stroma, and E, epithelium.

* The question in regard to the potential of cresyl violet arises from a lack of certainty as to whether the dye which we used was identical with that studied by Rapkine, Struyk and Wurmser (J. Chim. Phys. **26**: 340, 1929).

The test indicator is introduced into the stroma or epithelium of the ciliary body and allowed to come to equilibrium with the tissues. The degree of bleaching which takes place is observed under the microscope. Subsequently, an oxidizing agent, such as ferricyanide, is added, and the recovery of color is noted. The ratio of intensity of color before and after oxidation with ferricyanide affords a measure of the ratio of oxidant to reductant of the indicator in equilibrium with the tissue, and hence of the potential within the tissue. The recovery of color on oxidation is a necessary control demonstrating that the indicator has been reversibly reduced and not irreversibly destroyed. Experiments were conducted both aerobically and under conditions of asphyxia.

The results of these experiments are summarized in table 2. It can be seen that the potential in the epithelium in air is +0.100 volt, while that of the stroma in air is —0.130 volt, giving a difference of 0.230

10. Chambers, R.: An Analysis of Oxidation and Reduction of Indicators in Living Cells, in Cold Spring Harbor Symposia on Quantitative Biology, Cold Spring Harbor, L. I., New York, The Biological Laboratory, 1933, vol. 1, p. 205.

11. Cohen, B.; Chambers, R., and Reznikoff, P.: J. Gen. Physiol. **11**:585, 1928.

volt between the potentials of the two tissues. Under nitrogen both epithelium and stroma have the same potential, —0.290 volt. In the presence of 0.001 molar cyanide and air, the epithelium and stroma both have a potential of —0.200 volt.

Summary.—There is a difference in potential between the epithelium and the stroma (disappearing under asphyxia) which is capable of supplying the free energy for the electric current mentioned previously. In order to do so, the two parts of the tissue must be coupled by an electron carrier capable of accepting electrons from the stroma and transferring them to the epithelium. Before considering this electron carrier, we shall report briefly experiments relating to the enzyme systems involved in maintaining the difference in potential between the epithelium and the stroma.

III. THE ENZYME SYSTEMS

Since the metabolites of the stroma and epithelium are in all probability identical, the cause of the difference in potential between these two tissues is to be sought for in their enzyme systems.

A. OXIDASES

Seidel,[12] Schmelzer [13] and Samojloff [14] have shown that the ciliary epithelium gives an intense indophenol-oxidase reaction, whereas the stroma gives no reaction. We have confirmed and extended these observations. The technic is as follows:

A piece of tissue is placed on a microscope slide as described before and covered with about 1 cc. of Ringer's or buffer solution. This allows an easy access of oxygen for the reaction. To the bathing solution is added an equal volume of a freshly prepared solution of dimethylparaphenylenediamine and alphanaphthol (each 0.01 molar) in Ringer's solution. The development of the color of indophenol blue is observed under the microscope.

In the experiments the epithelium becomes intensely stained with indophenol blue while the stroma remains unstained. This indicates that indophenol-oxidase (Warburg's respiratory enzyme [15]) is present only in the epithelium and is absent in the stroma. The test for indophenol-oxidase is not a quantitative one, but gross changes in the activity of the enzyme manifest themselves in easily detectable changes in the rate of development of the color reaction. If the tissue is poisoned with cyanide, no color develops in the test though the reagent is not itself

12. Seidel: Ber. ü. d. Versamml. d. ophth. Gesellsch. **45**:14, 1925.

13. Schmelzer: Ber. ü. d. Versamml. d. ophth. Gesellsch. **45**:259, 1925.

14. Samojloff, A. J.: Arch. f. Ophth. **118**:391, 1927.

15. Warburg, O. H.: Ueber die katalytischen Wirkungen der lebendigen Substanz, Berlin, Julius Springer, 1928.

affected by cyanide.[16] Since the reagent is likewise unaffected by moderate changes in p_H, it is possible to use this test as an indication of the effect of p_H on the activity of the enzyme. The results of these experiments are shown in table 3. It is evident that a moderate increase in alkalinity over the normal physiologic p_H does not affect the activity of the enzyme, but that at p_H 6.9 the activity is reduced, while at p_H 6.2 it is almost entirely suppressed.

In addition to the indophenol-oxidase, we must consider other respiratory systems capable of reacting directly with oxygen. As noted in table 2, the potential of the tissue is 0.090 volt more negative under nitrogen asphyxia than it is under cyanide asphyxia in air. This indicates the presence in the tissue of substances other than indophenol-oxidase, capable of reacting directly with oxygen. However, these substances must be equal in effect in the epithelium and the stroma, since the potential under asphyxia is the same in both tissues.

TABLE 3.—*Variation of Indophenol-Oxidase Activity with* p_H

	Pyridine-Pyridine Acetate Buffers					
p_H	5.70	6.17	6.55	6.90	8.32	Ringer's Solution
Reaction	± ?	±	+	++	++++	++++

B. DEHYDROGENASES

In order that the postulated electric current can do a significant amount of work, the stroma must have sufficient reducing capacity. This capacity is determined by the substrates and the enzymes (dehydrogenases) [17] which activate them. The nature and concentration of the substrates determine the total reducing capacity of the tissue. Most of the substrates, however, have reducing ability only after activation by the dehydrogenases. The concentration of these enzymes, consequently, determines the active reducing capacity of the tissue. An attempt was

16. If the test is performed in the presence of a small volume of 0.001 molar cyanide, the tissue will at first remain entirely colorless, while in the control without cyanide the color develops rapidly. After the lapse of some time the color suddenly begins to appear in the tissue with cyanide and then develops as rapidly as it did initially in the control. This appearance of color in the tissue with cyanide can be prevented if the cyanide-reagent solution is frequently renewed. It is evident that the tissue is able to oxidize cyanide and recover from its toxic effects. We have noted a similar recovery from cyanide in regard to its effect on the penetration of acid and basic dyes, provided an overdose of cyanide is avoided.

17. Since these enzymes activate both the oxidant and the reductant, they might more properly be referred to as "metabolitases."

made, therefore, to estimate the concentration of dehydrogenases and substrates in the stroma. This was done by comparing the behavior of two basic dyes, methylene blue and crystal violet, one of which, methylene blue, can be reduced by the stroma and when reduced is electrically neutral. This comparison was made as follows:

If crystal violet in low concentration is introduced into the stroma, it is transferred rapidly and completely to the epithelium. When higher concentrations are used, the dye accumulates in the epithelium much more slowly. This difference in behavior with concentration is attributed to the fact that crystal violet is associated in concentrated solution (see Appendix). Methylene blue, on the other hand, although approximately equally associated, is transferred from the stroma to the epithelium equally well in dilute and concentrated solutions. This, in spite of the fact that when methylene blue is visible in the stroma the potential difference between the stroma and the epithelium is diminished and in spite of the further fact that under conditions when methylene blue is not reduced it is found to penetrate the tissue more slowly than crystal violet. For instance, crystal violet in the supravital technic stains the ciliary epithelium with great rapidity, while methylene blue stains slowly. This is not due to a difference in the staining ability, for with time an equal intensity of stain can be produced with either dye. Furthermore, at p_H 5.3, at which basic dyes penetrate from the epithelium to the stroma (see section IV), crystal violet passes with ease while methylene blue penetrates with great difficulty. On the other hand, when methylene blue is reduced the leuko form penetrates much more readily than does crystal violet. For instance, at physiologic p_H under asphyxia, crystal violet penetrates with difficulty or not at all, while methylene white penetrates with great ease, as can be shown by subsequent oxidation.

It was found that the oxidant of methylene blue passes through the stroma-epithelium barrier less readily than does crystal violet and the reductant penetrates much more readily than crystal violet. Since methylene blue is transferred from the stroma to the epithelium under physiologic conditions more readily than crystal violet, it is evident that it is transferred mainly in the reduced state. Since methylene blue, even in high concentration, is rapidly transferred from the stroma to the epithelium, it is evident that the rate of reduction in the stroma must be fast and, consequently, that there must be a high concenration of dehydrogenases and of substrates in the stroma. This inference is substantiated by a study of the secretory mechanism of the choroid plexus by one of us (R. D. S.) in association with L. Flexner.[17a]

The inactivation of the dehydrogenases, by a shift in p_H, may be compared with that of the indophenol-oxidase. Whereas under nitrogen, at physiologic p_H, safranine T is partially reduced by the stroma, at p_H 6.2 methylene blue is only partially reduced, and at p_H 5.7 even toluylene blue is only partially reduced. Since the concentration of metabolites is not changed, it follows that the dehydrogenases are inactivated at these p_H.

17a. Stiehler, R. D., and Flexner, L.: J. Biol. Chem., to be published.

Summary.—We may conclude that the difference in potential between the epithelium and the stroma is due, at least in part, to the presence in the epithelium of indophenol-oxidase and the absence of this enzyme in the stroma. Other oxidative enzymes are apparently distributed in the stroma and epithelium. Dehydrogenases are present in the epithelium and stroma. The potential difference between the epithelium and the stroma can be abolished by asphyxia, which affects the oxidase system or by acid p_H, which inactivates both the oxidase and the dehydrogenases. It is interesting to note that with the disappearance of the potential difference the ionic current described in section I likewise disappears. The remaining link in the postulated electric circuit, namely, the electron carrier, will be considered next.

IV. STROMA-EPITHELIUM BARRIER

Since the epithelium and the stroma are everywhere separated from one another by the stroma-epithelium barrier, it was natural to study this barrier and to see whether it could act as the electron conductor carrying electrons from the stroma to the epthelium. The first investigations were directed toward the influence of p_H on the physical chemical characteristics of this barrier.

A. p_H EFFECT AND ISOELECTRIC POINT

As has already been noted, when the potential difference between the stroma and the epithelium and the ionic current are abolished by asphyxia, the stroma-epithelium barrier shows a selective permeability in favor of acid and neutral dyes and a relative impermeability to basic dyes. It has likewise been noted that a slight shift toward higher acidity will produce the same effect. If the acidity is raised still higher, a point is reached where the permeability characteristics of the barrier to acid and basic dyes are reversed. This transition point will be called the isoelectric point of the barrier. The experiments on the effect of p_H on the barrier were performed as follows:

In order to test the effect of p_H on the barrier, it was first necessary to know how effectively the p_H of the tissue could be controlled by buffer solutions. Small portions of excised ciliary body were placed on glass slides and covered with from 1 to 2 cc. of various buffer solutions. After a few minutes a drop of p_H indicator (bromcresol green or bromcresol purple) was added, and the color in the tissue as well as in the bathing solution was observed under a microscope. Under the conditions of the experiment (p_H 5.3 to 7.0) these indicators were found to penetrate well into the epithelium and stroma. As nearly as could be determined, the same p_H existed on both sides of the barrier and in the surrounding fluid when buffers were used which had one species of the buffer system in the neutral or uncharged state, e. g., acetic acid–acetate, pyridine–pyridine hydrochloride and pyridine–pyridine acetate–acetic acid buffers. When buffers were used, both species of which were charged, e. g., phosphate and citrate buffers of p_H below

7.0, the p_H of the tissues was considerably higher than that of the surrounding fluid. Pyridine–pyridine acetate and acetic acid and acetate buffers were, consequently, selected for further study. The buffers were isotonic and contained calcium chloride, potassium chloride, magnesium chloride and potassium dihydrogen phosphate in the concentrations present in Ringer's solution. Buffer solutions between p_H 5.0 and 7.0 were made and their p_H determined electrometrically with a glass electrode. Standard acetate (0.1 molar acetic acid plus 0.1 molar sodium acetate) was used as the standard and assigned a p_H value of 4.620 at 25 C.

In testing the effect of p_H on permeability, an essentially similar technic was used in one set of experiments. Small portions of excised ciliary body were placed on a glass slide and covered with from 1 to 2 cc. of buffer of the desired p_H. After five minutes the buffer solution was drained off, and a minute drop of dye solution was placed near the edge of the tissue. When the epithelium had become stained, the excess of dye was removed, and the tissue was washed with the buffer and examined under the microscope for possible penetration of the dye into the stroma. In those experiments in which the observations had to be protracted for more than a few minutes, the evaporation of the buffer was avoided by having the tissue in a hollow ground slide under a cover slip.

In order to observe the penetration of dyes from the stroma to the epithelium, a more complicated procedure was used. The chest of an albino rabbit was opened, ether anesthesia being used, a cannula was inserted into the ascending aorta and the animal was perfused with Ringer's solution until the fluid returned clear. The perfusion was then halted. Both corneas were incised, and with the aid of a blunt spoon the lens and the vitreous were delivered, care being taken to avoid injury to the ciliary body. The ocular cavity was then irrigated for five minutes with a buffer solution (different buffers being used in the two eyes). At the end of five minutes, with the buffer solutions still actively irrigating the ocular cavity, a solution of the dye to be tested was injected through the perfusing cannula into the aorta, the injection being continued until the ocular blood vessels were well colored with the dye. The ciliary body and iris were then removed from each eye and dropped into a solution of the buffer with which it had been irrigated. Small slices still immersed in the same buffer solution were then studied under a microscope.

With decreasing p_H there is in the first part of the acid region a slight but definite decrease in the permeability of the stroma-epithelium barrier for both acid and basic dyes. This is associated with a slight shrinkage of the tissue. Throughout this zone of slight acidity (p_H 7.0 to 5.5) the barrier maintains the same selectivity as at physiologic p_H under asphyxia, being relatively impermeable to basic dyes but freely permeable to acid dyes (table 4). Between p_H 5.50 and 5.47 an abrupt change occurs, for at p_H 5.47 and lower the barrier is impermeable to acid dyes and freely permeable to basic dyes. At p_H 5.485 it is equally permeable to both acid and basic dyes. The same selective permeability of the barrier was found irrespective of whether the test dye was allowed to diffuse from the epithelium toward the stroma or in the reverse direction. It follows that the isoelectric point measured is that of the stroma-epithelium barrier and not that of any other substance.

Summary.—The selective permeability of the stroma-epithelium barrier for acid as against basic dyes is to be attributed to the electric charge inherent in the barrier, and the reversal of this selective permeability at p_H 5.50 to 5.47 indicates a reversal of the sign of the charge. At some point between p_H 5.50 and 5.47 the barrier must be without excess electric charge, i. e., isoelectric, a conclusion which is confirmed by the finding that selective permeability is absent at p_H 5.485. On the acid side of the isoelectric point, i. e., at p_H 5.47 and lower, the barrier is positively charged. On the alkaline side of the isoelectric point, i. e., at p_H 5.50 and higher, including physiologic p_H, the barrier is negatively charged.

B. OXIDATION-REDUCTION

The isoelectric point of the stroma-epithelium barrier was found neither to be fixed in position nor to have a definite breadth of zone. Instead it could be changed experimentally by oxidation and restored

TABLE 4.—*Determination of the Isoelectric Point of the Stroma-Epithelium Barrier; Effect of p_H on Penetration of Dyestuffs*

Acetic Acid-Acetate Buffers

	Penetration			
	Epithelium to Stroma		Stroma to Epithelium	
p_H	Acid Dyes	Basic Dyes	Acid Dyes	Basic Dyes
5.3	0	+	0	+
5.473	0	+		
5.486	+	+		
5.496	+	0		
5.7	+	0	+	0

to the original condition by subsequent reduction. This observation indicated that the barrier is a material substance, not merely a bounding surface, and that this barrier has as one component, at least, a reversible oxidation-reduction system. The presence in the barrier of such a system would enable it to act as an electron conductor capable of receiving electrons from the stroma and transferring them to the epithelium.[18] This property or action of the barrier is comparable to that of "mediators" which act normally in intracellular metabolism between two enzyme-substrate systems.

The only available method for studying the oxidation-reduction system of the stroma-epithelium barrier is to determine the shift in the isoelectric point (or the change in charge on the stroma-epithelium barrier) on oxidation. This was done by studying the selective permeability of the barrier to acid and basic dyes. In most experiments

18. The potentiality of the stroma-epithelium barrier to act as an electron conductor by virtue of a reversible oxidation-reduction system does not exclude the possibility of other, as yet unknown, mechanisms of electrical conduction.

the test dye was introduced into the epithelium. In a few experiments the dye was introduced into the stroma. The same results were obtained with both sets of experiments, proving that the effects observed were due to oxidation of the barrier and not of some other substance. By the use of this method, it was possible not only to study the effect of oxidation on the properties of the barrier but to measure roughly the characteristic potential (E'_o) of the oxidation-reduction system in the barrier. The experiments were performed as follows:

To test the effect of oxidation, three pieces of excised ciliary body were placed on slides. One piece of tissue was immersed in a buffer solution and the other two pieces in a buffer solution plus an oxidizing agent. After five minutes the oxidizing solution was removed from one of these pieces and replaced by a buffer solution containing a reducing agent. After five more minutes the oxidizing solution and the reducing solution were washed off with a buffer solution and the test stain was added to all three specimens. To test the effect of reduction, the same procedure was used except that buffer solutions containing a reducing agent were added to two of the three specimens at first, and one was subsequently oxidized. Ferricyanide, ferric chloride, iodine and quinhydrone have been used as oxidants and sodium hydrosulfate hydroquinone and a solution saturated with both quinhydrone and hydroquinone as reductants.

The effect of oxidation on the charge of the barrier was also studied by observing the movement of dyes from the stroma to the epithelium. Acid dyes were obtained in the stroma, with the epithelium clear, by injecting the dye intravenously, removing the iris-ciliary body as described previously and placing the tissue in Ringer's solution (the ionic current prevents the epithelium from staining). Slices of the tissue were placed on slides. A buffer solution (p_H 5.7) was added to some slices and a buffer solution plus an oxidant to others. After from five to ten minutes, some of the slices containing the buffer plus an oxidant were washed with buffer solution, and buffer plus hydrosulfite was added. Basic dyes were obtained in the stroma, with the epithelium clear, by irrigating the ocular cavity with a buffer solution (p_H 5.7) while injecting the dye as described previously. The tissue was treated as with acid dyes except that it was kept in a buffer solution in place of Ringer's solution. The choice of oxidant was difficult, since the oxidants, except ferric chloride, react with basic dyes. Iodine seemed the best to use, for although it precipitated the dye, precipitation was not complete. The tissue was observed in acetate buffers (pyridine reacts with iodine) with and without iodine. Care must be used not to allow the tissue to remain in the iodine solution for more than a minute or two since the iodine tends to be concentrated in the tissue and renders the dye more insoluble. The iodine was washed off with several changes of buffer solution, and the tissue was examined. The dye which penetrated into the epithelium in the presence of iodine was largely precipitated and hence gave only a feeble color. If a reductant was then added which reduced the excess iodine, the dye became soluble and stained the tissue brilliantly. The same results were obtained whether the penetration of dyes was studied from the epithelium to the stroma or vice versa.

As can be seen in table 5, all of the oxidants employed produce a reversal in the penetration of acid and basic dyes. Since the penetration of dyes depends on the electric charge on the stroma-epithelium barrier,

the charge must be reversed, demonstrating that the isoelectric point of the barrier has been shifted. This change in the charge on the barrier on oxidation can be completely reversed on subsequent reduction in the case of all the oxidants, showing that the oxidation-reduction system of the barrier is a reversible one and that the reaction is independent of the specific reagents employed.

In table 6 it is seen that the isoelectric point of the stroma-epithelium barrier is shifted by oxidation from p_H 5.485 to about p_H 6.6, whereas

TABLE 5.—*Influence of Oxidation and Reduction on the Stroma-Epithelium Barrier*

Acetate Buffer p_H 5.70

	Penetration of Dyes After			
	Oxidation		Reduction*	
Reagent	Acid Dyes	Basic Dyes	Acid Dyes	Basic Dyes
Control (no oxidant)	+	0		
Ferricyanide	0	+	+	0
Iodine	0	+	+	0
Quinhydrone	0	+	+	0
Ferric chloride	0	+	+	0

* The tissue is first oxidized by the reagent and then reduced with hydrosulfite.

TABLE 6.—*Shift of Isoelectric Point of Stroma-Epithelium Barrier by Oxidation*

Pyridine-Pyridine Acetate Buffers

	Penetration of Dyes Through Membrane			
	Membrane Reduced		Membrane Oxidized	
p_H	Acid Dyes	Basic Dyes	Acid Dyes	Basic Dyes
5.40	0	+	0	+
5.47*	0	+		
5.60	+	0	0	+
6.10	+	0	0	+
6.27	+	0	+	+
6.94	+	0	+	+
7.08	+	0	+	0
Ringer's solution	+	0	+	0

* Acetic acid-acetate buffer.

with reduction, no shift is observed (compare p_H 5.473 in table 4 with p_H 5.47 in table 6). It was noted in table 4 that the isoelectric zone of the barrier normally is less than 0.03 p_H units. Table 6 shows that in the oxidized state the zone covers between 0.7 and 1.0 p_H unit. Since the extent of the isoelectric zone is a measure of the slope of the acid-base titration curve in the vicinity of the isoelectric point, as shown later, it follows that the titration curve of the barrier normally and in the reduced state has a slope at least thirty times the slope of the curve for the oxidized state. This is not unusual, because oxidants generally have stronger acid and basic groups than the reductants, and, as is well known,

the stronger the acid-base groups in an ampholyte the wider the isoelectric zone. It is also not surprising to find that reduction causes no shift in the isoelectric point under these conditions. These conclusions are derived from the following theoretic considerations:

From the acid-base titration curves for the reductant and oxidant of an ampholyte containing a reversible oxidation-reduction system, e. g., the stroma-epithelium barrier, the relation between the isoelectric point and the degree of oxidation can be determined. Unfortunately, the actual titration curves are not known. However, an approximate relation can be calculated if the acid-base titration curves for both reductant and oxidant of the ampholyte are assumed to be linear in the p_H region between the isoelectric points of reductant and oxidant, as shown in figure 3 in which OX represents the titration curve of 100 per cent oxidant and RED that of 100 per cent reductant.[19] At the isoelectric point (pI) for the ampholyte partially oxidized, it follows that

$$(B^{+}_{o}) = K_o\ (pI_o - pI)\ a$$

$$(A^{-}_{r}) = K_r\ (pI - pI_r)\ (1 - a)$$

in which

(B^{+}_{o}) equals the excess cations of the oxidant

(A^{-}_{r}), the excess anions of the reductant

K_o, the slope of the titration curve of the oxidant

K_r, the slope of the titration curve of the reductant

pI, the isoelectric point for a mixture of oxidant and reductant

pI_o, the isoelectric point of the oxidant

pI_r, the isoelectric point of the reductant

a, the fraction in the oxidized state.

At any isoelectric point $(B^{+}_{o}) = (A^{-}_{r})$

or

$$K_o\ (pI_o - pI)\ a = K_r\ (pI - pI_r)\ (1 - a)$$

$$pI = \frac{K_r pI_r\ (1 - a) + K_o pI_o a}{K_r\ (1 - a) + K_o a}.$$

Let $M = pI_o - pI_r$, then

$$pI = pI_r + \frac{MK_o a}{K_r\ (1 - a) + K_o a}$$

or

$$\frac{pI - pI_r}{M} = \frac{\Delta pI}{M} = \frac{K_o a}{K_r\ (1 - a) + K_o a)} = \frac{a}{a + (1 - a)\ K_r/K_o}.$$

In figure 4, $\Delta\ pI/M \times 100$ (percentage of shift in the isoelectric point) is plotted against $100\ a$ (percentage of oxidation) for different ratios of K_r/K_o.

19. This assumption is one extreme of the possible titration curves and is approximated by substances having many acid and basic groups, e. g., proteins. The other extreme is obtained when each species has only one acid and one basic group, e. g., simple amino acids. Calculations made for both extreme cases lead to almost identical results. Since the latter type leads to an equation of the fourth degree with the attendant difficulties of calculation and presentation, only the simpler case is presented.

From the curves, it can easily be seen that when K_r is much larger than K_o, a small amount of oxidation produces little shift in the isoelectric point. The relative values of K_r to K_o can be determined from the width of the isoelectric zones as follows:

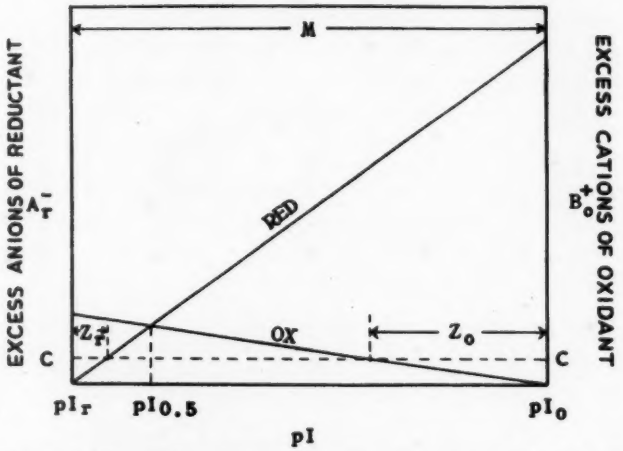

Fig. 3.—Diagram illustrating the relation between excess anions of reductant or excess cations of oxidant and shift in the isoelectric point.

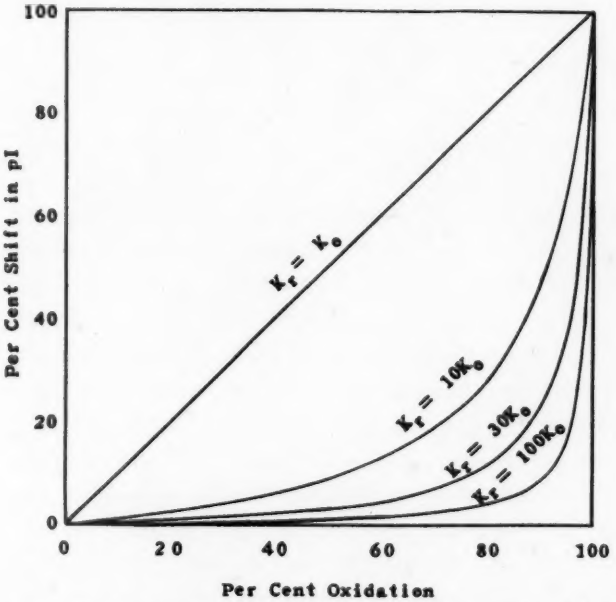

Fig. 4.—Chart showing a shift in the isoeletric point with oxidation.

In figure 2, C is assumed to be the excess charge necessary on the stroma-epithelium barrier, in any state of oxidation, to prevent the passage of oppositely charged ions. Z_r will then be equal to one-half the width of the isoelectric zone of the reductant and Z_o to one-half that of the oxidant. Since Z_r and Z_o are

inversely proportional to K_r and K_o, the ratio K_r/K_o will be equal to the ratio of the widths of the isoelectric zones of oxidant and reductant ($2Z_o/2Z_r$). The intersection of the titration curves of oxidant and reductant is the isoelectric point ($pI_{o.5}$) for 50 per cent oxidant plus 50 per cent reductant. It can be seen that this point will vary from pI_o when K_o equals ∞, through $\frac{1}{2}$ ($pI_r + pI_o$) when K_o equals K_r, to pI_r when K_o equals O (K_r remaining constant).

In the case of the stroma-epithelium barrier of the ciliary body, as stated before, the slope of the reductant is at least thirty times that of the oxidant ($K_r = 30\ K_o$) and probably not more than one hundred times that of the oxidant ($K_r = 100\ K_o$). If one observes these curves in figure 4, it is easily seen that it would not be possible to detect any oxidation of the stroma-epithelium barrier less than 25 per cent and, further, that 80 per cent of the shift in the isoelectric point occurs in the last 10 per cent of oxidation of the barrier. Consequently, the isoelectric point is most sensitive to changes in potential between 90 and 99.9 per cent oxidation of the stroma-epithelium barrier. This agrees with our observation.

TABLE 7.—*Determination of E_o' of Oxidation-Reduction System of the Stroma-Epithelium Barrier*

Pyridine–Pyridine Acetate Buffer p_H 6.6

Reagent	E_h at p_H 6.6 Volts	Penetration of Crystal Violet
Normal	.....	0
Ferricyanide	Over +0.420	+
Quinhydrone	+0.300	+
Saturated quinhydrone plus hydroquinone	+0.215	+
Saturated hydroquinone	+0.185	0

In table 7 it is significant to note that at p_H 6.6 oxidation of the stroma-epithelium barrier by quinhydrone allowed basic dyes to pass through the barrier. Reduction of the barrier with a saturated solution of hydroquinone ($E_h = +0.185$ [20]) restored the original selective permeability; whereas, a solution saturated with both hydroquinone and quinhydrone ($E_h = +0.215$) did not. Therefore, at p_H 6.6 and at some potential (E_h) of the stroma-epithelium barrier between +0.185 and +0.215, the selective permeability of the barrier to basic dyes is removed. This reversal in permeability to basic dyes occurs at the upper limit of the isoelectric zone, as shown before. It can be shown that the shift in the limit of the isoelectric zone is proportional to the shift in the isolectric point itself. From the information derived on the relation between the isoelectric point and percentage of oxidation, the degree

20. This is the minimum value of the potential measured. It is obvious that the hydroquinone solution must have contained traces of quinone. Since this solution was used as a reductant, the potential established in the tissues cannot be less than the measured potential. If the potential in the tissues is higher, the error in measuring the potential of the stroma-epithelium barrier is correspondingly reduced.

of oxidation (a) of the stroma-epithelium barrier, corresponding to a shift in the upper limit of the isoelectric zone to p_H 6.6, is calculated to be between 98 and 99.5 per cent.

The necessary information required to calculate the E'_o of the oxidation-reduction system of the stroma-epithelium barrier from the values of E_h and a is not available. However, if it is assumed that the system in the stroma-epithelium barrier can be treated as similar systems in aqueous solution and that neither reductant nor oxidant are associated, the value of E'_o can be calculated from the equation:

$$E_h = E'_o + \frac{RT}{nF} \ln \frac{a}{1-a}.$$

The validity of these assumptions must remain questionable.

One the basis of the assumption that the oxidation-reduction system of the stroma-epithelium barrier involves two electrons (a one electron system would be more favorable for the present argument), the E'_o at p_H 6.6 is $+0.140 \pm 0.025$ volt (the error considers only the errors in the determination of E_h and a and not those inherent in the assumptions). It is not possible to determine the E'_o of the system at physiologic p_H since the $E'_o : p_H$ curve is not known. It is reasonable to assume that the slope of the curve is no greater than 0.06. If a 0.03 slope is assumed, then E'_o equals $+0.115 \pm 0.050$ volt at p_H 7.4. The additional uncertainty of ± 0.025 volts is added to allow for a 0.00 slope or a 0.06 slope. The potential of the epithelium at this p_H is estimated to be $+ 0.100 \pm 0.015$ volts (see section II). If the assumptions are valid, then, under physiologic conditions the stroma-epithelium barrier would be oxidized partially by the epithelium or reduced completely by the stroma.

Summary.—The isoelectric point of the stroma-epithelium barrier is shifted by oxidation and restored to the original position by subsequent reduction. Therefore, the barrier has as one of its components, at least, a reversible oxidation-reduction system. The isoelectric zone is wider in the oxidized state than in the normal and reduced states. From the data on the shift of the isoelectric point and the width of the isoelectric zones, together with the potential of an incompletely oxidized stroma-epithelium barrier measured at one limit of the isoelectric zone, the E'_o of the oxidation-reduction system is calculated with the aid of certain assumptions to be $+0.140$ volts at p_H 6.6. From this potential it is inferred that the epithelium normally tends to oxidize the membrane partially, whereas the stroma tends to reduce it. Consequently, electrons can be received by the barrier from the stroma and transferred to the epithelium by virtue of the reversible oxidation-reduction system of the barrier. All the elements necessary for an electric current to exist have been demonstrated. This current can produce useful work. One form of work is in the transfer of water, which will be considered next.

V. TRANSFER OF WATER

The present investigation had its origin in the discovery that the ciliary body was irreciprocally permeable to water. Since the movement of water in the transparent and watery tissues of the eye cannot readily be observed, we have been forced to study first the movement of substances that we could see, namely, dyes. In what way can the knowledge gained regarding the mechanism of the transference of dyes in the ciliary body be applied to the problem of transfer of the water? The passage of an ionic current through the pores of an electrically charged membrane is associated with the transfer of water through the membrane. This phenomenon has been known and studied for over a century and is called electroendosmosis. It has been shown that if the membrane is positively charged, the flow of water is in the same direction as that of the anions; if the membrane is negatively charged, the flow of water is in the same direction as that of the cations. Since the ciliary stroma-epithelium barrier is negatively charged at physiologic p_H, the endosmotic flow of water through the barrier must be in the same direction as that of basic dyes, namely, from the stroma to the epithelium.

The mechanism by which water is transferred across a membrane under the influence of an electric current has not been adequately determined. The generally held theory assumes that the applied current moves the water directly. Bethe's [21] experiments suggest that the current leads to an accumulation of ions on one side of the membrane and that the water is moved osmotically. For our present purpose it is immaterial whether one or the other of these hypotheses is correct. It is, however, possible to show that water can be transferred across the ciliary stroma-epithelium barrier in appreciable quantities by an artificially applied electric current as follows:

The experiment was performed as follows (fig. 5): A glass cannula filled with Ringer's solution was introduced into the vitreous of each eye of a rabbit, ethyl carbamate anesthesia being used. Each cannula was connected by a T tube to a horizontal capillary tube containing a bubble of air and thence to a reservoir of Ringer's solution, the capillary to serve as a flow meter. The other arm of each T tube contained a zinc–zinc sulfate nonpolarizable electrode, the zinc sulfate solution being separated from the Ringer's solution by an agar plug. At the onset of the experiment the level of the reservoirs of Ringer's solution was raised to a point slightly above the normal intraocular pressure, so that a slow movement of the bubble in each capillary toward the eye was observed. An electric current was then applied to the two zinc electrodes, and any change in the direction or velocity of movement of the bubbles in the flow meters was recorded.

It was found that when sufficient potential (20 volts or more) was applied, the solution flowed into the eye from the reservoir attached to

21. Bethe, A., and Toropaff, T.: Ztschr. f. phys. Chem. **39**:597, 1915.

the positive electrode, and fluid came out of the eye attached to the negative electrode (fig. 5). In the latter case the direction of the ionic current was the same as that which we have observed normally under the influence of the difference in potential which exists between the two sides of the ciliary stroma-epithelium barrier. When the direction of the current was reversed, the direction of flow in the flow meters was promptly reversed.

If the animal's eyes were removed after a short flow of current and fixed and sectioned, it was found that the ciliary body in the eye that had been attached to the positive electrode was normal in appearance,

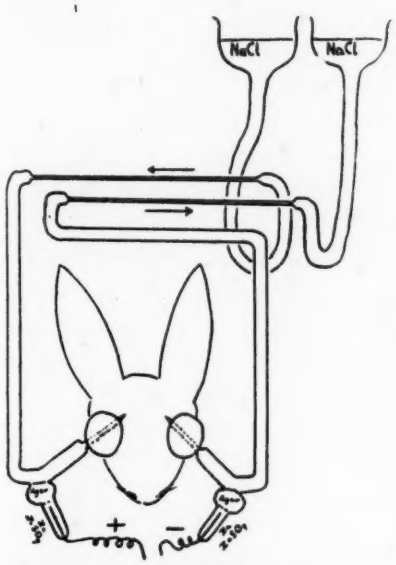

Fig. 5.—Schematic diagram of apparatus used in the electroendosmosis experiment.

while in the eye attached to the negative electrode the ciliary capillaries were engorged and tightly packed with corpuscles. It would appear that fluid had been withdrawn from these capillaries into the interior of the eye at so rapid a rate as to result in an inspissation of the blood within the capillaries and a consequent congestion of these vessels.

Summary.—These experiments show that the electrical mechanism responsible for the transfer of dyes in the ciliary body is adequate to explain also the transfer of water in this tissue. The experiments here reported are sufficient to show that this secretory mechanism may, in fact, be operative in the ciliary body. Conclusive proof that this mechanism is actually operating and that if operating it accounts quantitatively for the secretory activities of the ciliary body is lacking.

VI. OTHER COMPONENTS OF THE BLOOD-AQUEOUS BARRIER

A. CAPILLARY WALL

The blood-aqueous barrier in the ciliary body is composed of three different membranes: the capillary endothelium, the stroma-epithelium barrier and the epithelial cell membrane. In the course of the experiments described numerous dyes have been injected intravascularly into albino rabbits, and the iris and ciliary body were then examined under the microscope. It was observed that none of the basic dyes used penetrated the walls of the capillaries of the iris, while all entered the ciliary stroma with ease. The acid dyes penetrated the capillaries of the iris slowly and feebly, while they penetrated the ciliary stroma with ease.

Summary.—The ciliary capillaries are much more permeable than either the capillaries of the iris or the stroma-epithelium barrier.

B. EPITHELIAL CELL MEMBRANE

The question may be raised as to whether the structure that we have called the stroma-epithelium barrier is identical with the cell membrane on the surface of the second layer of epithelium facing the stroma. While it is plain that this part of the cell membrane must form part of the barrier between the cytoplasm of the epithelium and the reticulum of the stroma, it is evident from the experiments reported that those parts of the epithelial cell membrane that are available for separate observation show entirely different permeability characteristics from the stroma-epithelium barrier. At p_H higher than the isoelectric point of the barrier, both acid and basic dyes diffuse readily into both layers of epithelium, while only acid dyes penetrate the stroma-epithelium barrier. At p_H lower than the isoelectric point of the barrier, both acid and basic dyes continue to diffuse readily into both layers of epithelium, while only basic dyes penetrate the stroma-epithelium barrier. Also, we have found no evidence of polarity in the cell membrane of the first layer of epithelium in which both the free surface and that adjoining the second layer were adequately studied. If the basal layer of the epithelial cell membrane is identical with what we have called the stroma-epithelium barrier, it is different from either the intercellular or the superficial membrane of the epithelial cells.

Summary.—The stroma-epithelium barrier is the least permeable of the three anatomic barriers between the blood and the aqueous in the ciliary body, hence the limitations in permeability of the stroma-epithelium barrier form the determining factor in the whole system.

COMMENT

The present investigation was undertaken with the aim of discovering the secretory mechanism of the ciliary body. We have found that the respiratory metabolism of the epithelium differs from that of the stroma. This difference is due to the presence of Warburg's respiratory enzyme in the epithelium and the absence of this enzyme in the stroma. Owing to this distribution of the oxidase, there is a difference in potential between the epithelium and the stroma which gives rise to an electric current carrying cations from the stroma to the epithelium and anions from the epithelium to the stroma. This ionic current will transfer water from the stroma to the epithelium. The electric circuit is completed by an electron transfer through the stroma-epithelium barrier, presumably through the reversible oxidation-reduction system of this barrier. Under conditions which cause the potential difference between the epithelium and the stroma to disappear, the electric current disappears. It is interesting to note that the irreciprocal permeability of the ciliary body to water reported previously [1] disappears under conditions which abolish the potential difference and the electric current.

The secretory mechanism which we have described should not, we believe, be thought of as solely responsible for the formation of the intraocular fluid. Variations in the permeability of the ciliary capillaries, in the osmotic pressure of the plasma proteins and in the excess of pressure in the ciliary capillaries over the intraocular pressure must largely control the amount of fluid which enters the stroma of the ciliary body and is available for transfer into the ocular cavity.

SUMMARY

Between the stroma and the epithelium of the ciliary body there is a barrier which, under certain conditions, shows a selective permeability in favor of acids as against basic dyes. This barrier is negatively charged at physiologic p_H and has an isoelectric point at p_H 5.485. The permeability of the barrier is increased by the absence of calcium. The barrier is capable of reversible oxidation and reduction. Depending on the validity of certain assumptions, the E'_o of the oxidation-reduction system in the barrier is +0.140 volt at p_H 6.6. Under physiologic conditions the barrier tends to be partially oxidized by the epithelium and to be reduced by the stroma.

The epithelium of the ciliary body contains indophenol-oxidase. The stroma does not contain this enzyme. Other oxidases are probably equally distributed in these tissues. Both tissues contain dehydrogenases. Related to the unequal distribution of the indophenol-oxidase there is a difference in potential between the epithelium and the stroma of 0.230 volt. The potential of the epithelium is +0.100 volt. The potential of the stroma is —0.130 volt.

The ciliary body shows an irreciprocal permeability to water and to certain acid and basic dyes, transferring water and basic dyes from the stroma to the epithelium, i. e., from the blood to the aqueous, and transferring acid dyes in the reverse direction.

It is postulated that the mechanism of the irreciprocal permeability of the ciliary body depends on an electric current which transfers water and cations from the stroma to the epithelium and anions from the epithelium to the stroma. The source of energy for this electric current is supplied by the differences between the oxidative and the reductive processes in the epithelium and stroma. The electric circuit is completed by an electron transfer through the stroma-epithelium barrier, presumably through the reversible oxidation-reduction system of the barrier.

APPENDIX

In the course of the investigation reported here many dyes beside those mentioned were used. Many of these were found unsuited for the purposes of our study because of poor color, poor staining quality, poor penetration, irreversible destruction in the tissue or excessive toxicity (staining of nuclei). These and certain other characteristics of the dyes used are listed in table 8. The azo dyes were not included in the table, since they are generally toxic and do not penetrate or stain the epithelium easily. The dyes that were found most satisfactory and that were, therefore, used for most of the experiments were crystal violet (basic dye), bromphenol blue and rose bengal (acid dyes) and rhodamine B (neutral dye).

In order to interpret the behavior of the dyes in the tissue it would be necessary to know their physical chemical characteristics. Unfortunately, little such information is available in the literature. Data on the molecular size or volume, molecular shape, hydration, etc., are still wanting. Some of the observations on the behavior of the dyes in the tissue are explained by the properties of these dyes, discussed later.

A. IDENTIFICATION OF THE DYES

Commercial dyes sold by different manufacturers under the same name are often different dyes. Furthermore, dyes as sold often are not one chemical substance but contain impurities and isomeric substances. In order to identify the dyes used in these studies, the Color Index number and the manufacturer are listed in table 8. Dyes not obtained commercially were obtained through the courtesy of the department of physiologic chemistry or synthesized in our laboratory.

B. ASSOCIATION

Holmes [22] has shown that the absorption spectrums of many dyes shift with changing concentration of the dye. Cohen and Preisler [23] found in the case of the oxazine dyes that the oxidation-reduction potentials shifted with the shift of the absorption spectrums and suggested that association (polymerization) of the oxidants would explain this phenomenon. Stiehler and Clark,[24] by studying

22. Holmes, W. C.: Indust. & Engin. Chem. **16**:35, 1924.

23. Cohen, B., and Preisler, P. W.: Studies on Oxidation Reduction: XVI. The Oxazines: Nile Blue, Brilliant Cresyl Blue, Methyl Capri Blue, and Ethyl Capri Blue, Pub. Health Rep., 1931, supp. 92.

24. Stiehler, R. D., and Clark, W. M.: J. Am. Chem. Soc. **55**:4097, 1933.

TABLE 8.—*Data on Dyes Used in Experiments*

Dye*	Color Index No.	Chemical Type	Associated in Concentrated Solution‡	Comment
		Cations in Solutions		
Crystal violet (NAC).....	681	T.P.M.†	Yes	Described in text and appendix
Malachite green (NAC).....	657	T.P.M.	?§	Like cystal violet but penetrates stroma-epithelium barrier more readily
Basic fuchsin (NAC).....	677	T.P.M.	No?	Poor stain; poor color; low solubility
Night blue (Gr).....	731	T.P.M.	Yes	Extremely low solubility in salt solutions; otherwise like crystal violet
Victoria blue (NAC).....	729	T.P.M.	Yes	
Methyl green (Gr).....	685	T.P.M.	No?	Filled stroma when injected intravenously; stained epithelium a feeble violet instead of green
Toluylene blue (Lab).....	820	Indamine	?	Penetrated stroma-epithelium barrier in both directions aerobically, probably as reductant
Bindschedler's green (BDH).	819	Indamine	?	
Methylene blue (HWD).....	922	Thiazine	Yes	Described in text
Lauth's violet (NAC).....	920	Thiazine	Yes	Like methylene blue
Cresyl blue (NAC).....	877	Oxazine	Yes	Like methylene blue
Cresyl violet (NAC).....	...	Oxazine	?	Oxidant like crystal violet; reductant like leukomethylene blue
Dimethylphenosafranine (NAC)	842	Azine	Yes	Like methylene blue except not reduced in stroma in air accumulated in epithelium slowly
Safranine T (?).....	841	Azine	Yes	Like dimethylphenosafronine; poor color
		Anions in Solution		
Bromphenol blue (HWD)....	...	Sulfonphthalein	No	Described in text; feeble stain
Eosin Y (?).....	768	Fluorone	No	Good stains; penetrated stroma-epithelium barrier like bromphenol blue; eosin penetrates barrier more easily than the others; see appendix on charge in acid solutions
Erythrosine (?).....	773	Fluorone	No	
Phloxine (NAC).....	778	Fluorone	No	
Rose bengal (PCL).....	779	Fluorone	No	
Uranin (?).....	766	Fluorone	Yes	Poor stain; poor color; penetrates stroma-epithelium barrier easily
Acid fuchsin (?).....	692	T.P.M.	?	Poor stain; poor color; irreversibly destroyed in tissue
Fast green F. C. F. (NAC)..	...	T.P.M.	?	Poor penetration into epithelium; poor stain
Bromcresol green (HWD)...	...	Sulfonphthalein	No	Like bromphenol blue; partially as free acid in acid solutions; see appendix
Bromcresol purple (HWD)..	...	Sulfonphthalein	No	
2,6 dichlorophenolindophenol (Lab)	...	Indophenol	No?	Easily reduced– in acid solutions, free acid present and irreversibly destroyed
Indigo disulfonate.....	1180	Indigo	No ?	Poor stain; like bromphenol blue except penetrates stroma-epithelium barrier more slowly
Indigo trisulfonate (Lab)...	...	Indigo	Yes?	
		Neutral in Solution		
Rhodamine B (NAC).....	749	Fluorone	Yes	Described in text and appendix; penetrated stroma-epithelium barrier rapidly under all conditions
Pyocyanine (HLaR).....	...	Azine	?	Poor stain; low solubility; reduced in stroma

* (NAC), National Aniline & Chemical Co., Inc.; (Gr) Groubler; (BDH), British Drug Houses Ltd.; (HWD), Hynson, Westcott & Dunning, Inc.; (PCL), Providence Chemical Laboratories; (HLaR), Hoffmann-LaRoche, Inc.; (Lab), laboratory sample; (?), manufacturer unknown.

† T.P.M. indicates triphenyl methane dye.

‡ The data are taken mainly from Holmes.[22]

§ The question mark means that no information is available or that data are not conclusive.

the distribution of the dye between two immiscible solvents, were able to show in the case of one of the aposafranines that association of the oxidant occurred.

The absorption spectrum of crystal violet in aqueous solution shifts with concentration,[22] but there is no shift with concentration in amyl acetate solutions. We have, therefore, studied the distribution of crystal violet between water and amyl acetate. The results show that in amyl acetate only one species of the dye exists, whereas in water this species and its dimer are present. Determinations of the freezing point on 0.01 molar solution of crystal violet in water indicate a molecular weight of about 1100 (molecular weight of $C_{25}H_{30}N_3Cl + 9H_2O = 570$).

The distribution experiments show that in 0.01 molar solution over 99 per cent of the dye exists as dimer. Consequently, in concentrated aqueous solutions two molecules of the dye associate and in the amyl acetate solutions only the monomer exists. The association constant was found to be about 2×10^{-8} in water; about 2×10^{-6} in 0.15 molar sodium chloride solution. The effect of ionic strength on the association constant is similar to that found with sulfonated rosindone.[24]

This phenomenon of association makes possible the interpretation of the following observations: When the ionic current in the ciliary body is abolished (asphyxia or p_H 6.0), crystal violet in 0.001 molar solution fails to penetrate the membrane. If 0.00001 molar solution is used, penetration slowly takes place. When the ionic current is not abolished, the dye is transferred from the stroma to the epithelium. If low concentrations are used, the accumulation of the dye in the epithelium is rapid. When high concentrations are used, the accumulation is much slower. With varying concentrations pictures intermediate between these extremes are obtained. Since even in concentrated solutions of the dye a small fraction is present as monomer, it is possible that only the monomer can pass through the membrane. Many of the other dyes that we have used also show this phenomenon of association (table 8).

C. IONIC CHARGE AND RELATIVE MOBILITY

The ionic charge and the relative mobilities of the dyes were determined by observing the movement of the dyes under an electric current. The dyes were dissolved in 0.01 molar buffers. The dye concentration was 0.001 molar. The resulting classification of anions cations and neutral particles is shown in table 8. The behavior of all of the dyes was the same as predicted from their chemical structure except rhodamine B. This dye is generally classified as basic and would, therefore, form cations in solution. The sample, obtained from the National Aniline & Chemical Co., was alleged to be the chloride. The sample did not contain chloride, and the dye did not migrate under the influence of an electric current. The dye is, therefore, electrically neutral and is probably a zwitterion in solution. The mobilities of all of the other dyes did not differ from one another by more than a factor of two. Consequently, the differences in penetration of these dyes in the tissue cannot be explained on the basis of their mobilities.

In buffers of low p_H some of the acid dyes exist partially as the free undissociated acid and hence behave as neutral substances. At physiologic p_H these dyes exist only as the anion or dissociated acid in solution.

COLOBOMA OF THE OPTIC NERVE AND OF THE MACULA

A MICROSCOPIC STUDY

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AND
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Colobomas of the optic nerve and of the macula are among the more interesting of ocular anomalies. The literature contains many clinical descriptions but relatively few anatomic studies of these defects. Caspar [1] in 1887 classified colobomas of the nerve clinically on the basis of the arrangement of the blood vessels as they emerged from, and distributed themselves on, the disk. It was soon learned, however, that there was little correlation between the microscopic structure and the appearance of the fundus and that wide differences existed in the cases in which anatomic study was possible.

Most authors agree that colobomas are due to faulty development in the elements comprising the tissue "anlage." Often these tissues are modified or replaced by other tissues, and alterations may occur in tissues surrounding the coloboma as well. Coloboma of the nerve is due to anomalous closure of the fetal cleft and occurs in its upper end. The defect has been ascribed by some to primary aberrations in the epiblastic layer of the optic cup and by others to alterations primarily in the mesoblastic tissue. Faulty development of the inner and outer layers of the optic cup and stalk, infolding of the primary layers, as well as the interpolation of vascular or other mesodermal tissue, and the alterations that may be present as the result of the pluripotentiality of the cells in the margin of the everted secondary optic vesicle are mentioned as factors influencing the formation of the immediate tissue about the nerve as well as of the nerve itself. Other factors, such as ingrowth of the nerve fibers of the retina into the primordial optic nerve stalk and the influence of one tissue develop-

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From the Laboratories and Ophthalmological Division of the Mount Sinai Hospital.

1. Caspar, L.: Ueber das Colobom des Sehnerven, Dissert., Bonn, J. Bach Wwe., 1887; Zur Kenntnis der angeborenen Anomalien der Sehnervenpapille, Arch. f. Auengh. **32**:12, 1896.

ment on another, are further explanations offered for the structural peculiarities seen in cases of coloboma of the optic nerve.

Colobomas of the nerve vary from almost complete absence of the nerve to modified degrees of excavations and "filled-in" ectasias of the

Fig. 1.—Drawing of the left fundus showing the coloboma of disk, temporal myopic crescent and macular retinal atrophy.

Fig. 2.—Section through the disk, indicating ectasia of the dura and sclera at the posterior pole and enlargement of the diameters of the globe.

nerve head. The peripheral portion of the nerve structure may be involved. Included, perhaps, are the crater-like holes of the optic disk and disks with the type of inferior conus described by Fuchs.[2]

2. Fuchs, E.: Ueber die Lamina Cribrosa, Arch. f. Ophth. **91**:435, 1916.

Coats [3] in 1908 reviewed the literature dealing with instances of congenital defects of the nerve and concluded that only a few were true colobomas. Coats,[3] Parsons [4] and Duke-Elder,[5] although of the opinion that the relative differences may be a question of didactic interest only, have defined the criteria for such congenital anomalies of the optic nerve. According to these authors a true coloboma of the optic nerve is one in which there is absence of a communication between the intervaginal space and the coloboma; i. e., the ectasia must lie wholly within the sheaths of the optic nerve. Also, a definite boundary must exist between the choroid and the colobomatous area. Coloboma of the choroid adjacent to the optic nerve and involving the latter is therefore not included within this grouping. Furthermore, in a true coloboma the central artery of the retina is found to course through the nerve head itself.

Colobomas of the macula have been described. Microscopically, the macula may be almost entirely replaced by unorganized tissue or consist of either cystic cavities or be represented by a hole. Although the macula is not derived from the primary fetal fissure, some authors consider macular coloboma to be an associated growth anomaly accompanying abnormal closure of the fetal cleft. Subsidiary fissures continuous with the primary cleft have been described. When not connected with the primary fetal fissure, the coloboma is considered atypical. According to Mann [6] all colobomas of the macula are acquired. She expressed the belief that the maculas in those cases considered as colobomatous were injured during fetal life by trauma or inflammation. Sorsby,[7] among others, however, has described cases of congenital macular coloboma in which the condition not only was familial but was often present bilaterally.

REPORT OF A CASE

History.—Mrs. S. J., aged 40, was admitted to the medical ward of the Mount Sinai Hospital with a diagnosis of hypertensive renal disease. The fundus of the right eye revealed hypertensive retinitis. The left eye was highly myopic, with vision reduced to perception of light. The media were clear. The disk was

3. Coats, C.: The Pathology of Coloboma of the Nerve Entrance, Roy. London Ophth. Hosp. Rep. **17**:178, 1908.

4. Parsons, J. H.: Pathology of the Eye, London, Hodder & Stoughton, 1906, vol. 2, p. 824.

5. Duke-Elder, W. S.: Textbook of Ophthalmology, St. Louis, C. V. Mosby Company, 1938, vol. 2, pp. 1256 and 1261.

6. Mann, I. C.: Certain Abnormal Conditions of the Macular Region Usually Classed as Colobomata, Brit. J. Ophth. **11**:99 (March) 1927.

7. Sorsby, A.: Congenital Coloboma of the Macula, Together with an Account of the Familial Occurrence of Bilateral Macular Coloboma in Association with Apical Dystrophy of the Hands and Feet, Brit. J. Ophth. **19**:65 (Feb.) 1935.

roughly oval, uniformly gray and from two to three times normal size. Its surface was slightly depressed, but further details of depth and markings could not be ascertained. All of the vessels sprang from the edge of the disk and turned sharply into the retina much in the manner of cilioretinal arteries and opticociliary veins. A large crescent bordered the disk temporally. The macular area was the seat of discrete areas of atrophy, probably of myopic origin. The

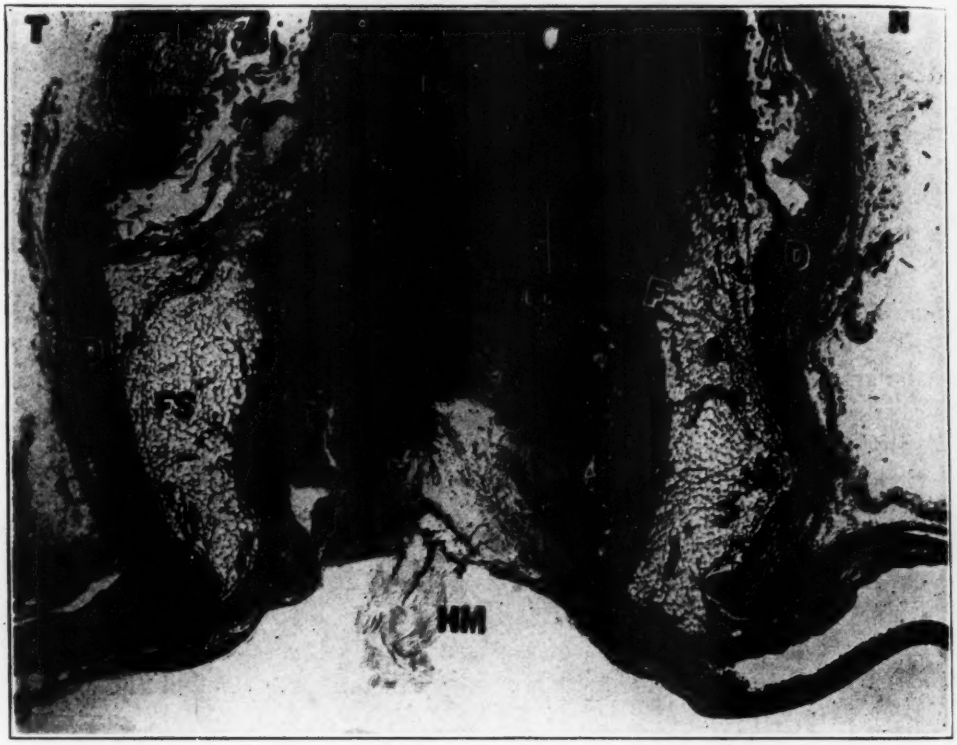

Fig. 3.—Section of the nerve through the approximate center of the disk. *T* is the temporal and *N* the nasal side of the nerve. Above is the normal nerve with the central retinal artery. The points in the nerve indicated by *LC* correspond to the upper and lower limits of the lamina cribrosa. The pia, *P*, and arachnoid, *A*, terminate midway between these levels and merge with the dura, *D*. There are thus a true intervaginal space, *TS*, and a false intervaginal space, *FS*. The upper fibers of the lamina cribrosa arch abruptly downward, especially temporally. They emerge as strands into the false space and can be traced down toward the scleral promontory, *SP*. Some are attached to the dura, *DL;* others are attached as fragments to the edge of the nerve, *F*. The false space contains, in addition to fragments of the lamina cribrosa, a loose syncytium of dural fibers and blood vessels derived from the central retinal artery. In front of the lamina cribrosa is the undifferentiated portion of the nerve, *UN*, consisting of central fibrillar and outer cellular zones, bordered on either side by a dural sheath, *S*, rich in elastic fibers. The central zone is continuous with the remnants of the hyaloid membrane, *HM*. The choroid is poorly developed temporally. Nasally, vessels in the false space enter the choroid, which is well developed on this side. No retinal vessels are seen in the disk at this level.

diagnosis was coloboma of the optic nerve in a highly myopic eye. Study of the visual fields could not be done on account of the condition of the patient. Death occurred ten days after her admission to the hospital.

Ocular Findings.—The left eye, together with 15 mm. of the nerve, was removed six hours after death. The cut end of the nerve was normal in size, but the vaginal space was considerably wider than normal. At the junction of the nerve and the sclera was a prominent ectasia of sclera, especially nasally. The measurement from this point to the corneal limbus was 33.5 mm.; the circumference of the outer nerve sheath at the sclera was 26 mm., 6 mm. larger than this circumference in the average normal globe.

Fig. 4.—The undifferentiated nerve. *F* is the loose fibrillar, relatively acellular tissue connected with the hyaloid membrane, *HM*; *HA*, the endothelium of the hyaloid artery; *S*, sheaths of the hyaloid structure. The tissue, *C*, contains large neuroglia cells, immature glia fibers, cystic spaces and pigment. *SH* is a reflection of dura, forming a sheath for the undifferentiated nerve.

Fixation of the globe was done in Bouin's solution, and serial section were prepared in pyroxylin and paraffin and were stained with hematoxylin and eosin, Van Gieson's stain and Weigert's elastica.

Microscopic Structure.—Globe: The anterior portion of the globe was normal except for a moderate degree of myopic stretching. In the retina, temporal to the macula, there were a few cystic spaces in the outer layers.

Colobomatous Area: The scleral canal was considerably widened, the distance between the scleral promontories measuring 3.5 mm. The section through the approximate center of the nerve revealed a large defect at its bulbar end. Here the nerve was replaced by a poorly developed undifferentiated tissue. This tissue was arranged in three zones as follows: 1. Centrally there was a loose fibrillated syncytium, which stained poorly with eosin and was practically avascular and

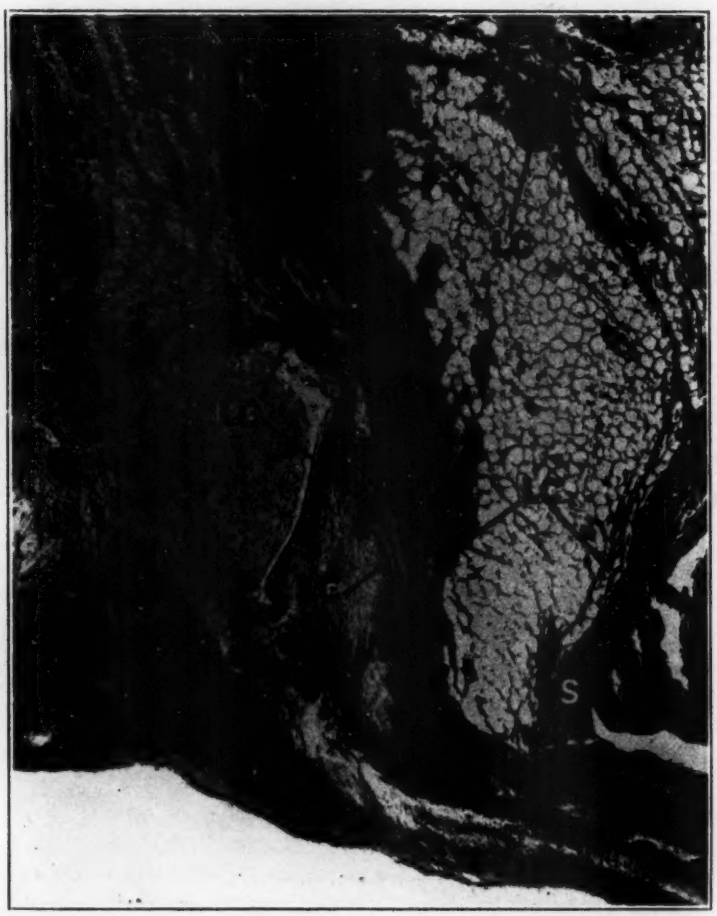

Fig. 5.—Section stained with Weigert's elastica to show splitting of the elastic lamina, *LC*, as it crosses upward toward the definitive nerve. Some of the fibers are attached to the scleral promontory, S; others can be seen in the dural sheath, lining the undifferentiated nerve.

acellular. 2. Extending from this central tissue, and for 1.5 mm. laterally and backward, was a poorly organized mass of nerve tissue, the periphery of which consisted of irregular bundles of nerve fibers intermingled with poorly stained nerve septum fibers and large glial cells. Among the nerve bundles were irregular cystic spaces of various sizes. The poorly developed nerve tissue was continuous with the retina anteriorly and with the true nerve posteriorly. 3. The peripheral

zone consisted of a broad sheath which was continuous with the pia posteriorly and merged at its bulbar attachment with the chorioretinal tissue. The inner aspect of this sheath was lined with masses of pigment resembling pigment epithelial tissue.

Behind this mass of undifferentiated tissue there was an abrupt transformation of the definitive nerve at the lower border of the lamina cribrosa. The central acellular tissue was continuous with a membranous mesenchymal structure, which projected for about 1.5 mm. into the vitreous, stained somewhat lighter and was more homogeneous than the structure in the disk. In the center of this tissue was an endothelial lining, undoubtedly a remnant of the embryologic hyaloid vascular system. For a short distance in the vitreous this structure was bordered by a sheath of glial tissue.

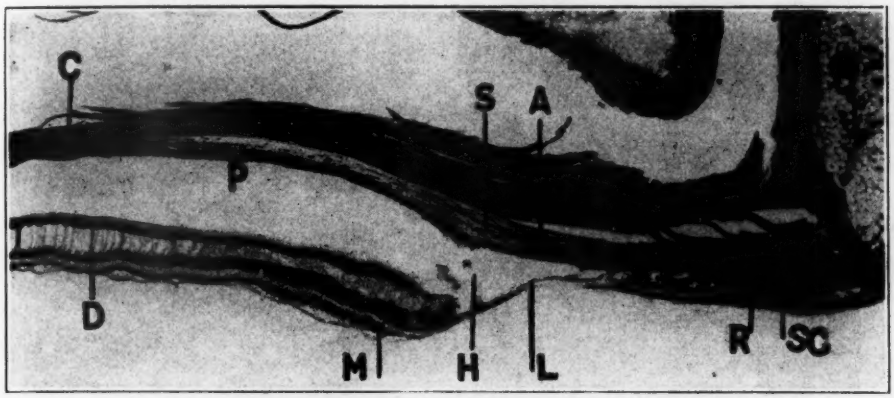

Fig. 6.—Partial choroidal-macular coloboma. *C* indicates the normal choroid with pigment epithelium, *P*; *S*, absence of the choroidal structure with replacement by elastic fibers; *A*, absence of pigment epithelium; *D*, cystic degeneration of the retina adjoining the macula; *M*, the macula; *H*, a hole in the macula; *L*, the internal limiting membrane, and SC, a portion of sclera enclosing layers of retinal pigment, *R*.

Lamina Cribrosa: The most anterior limit of the laminated fibers was situated 2 mm. behind the point where the hyaloid artery entered the hyaloid sheath and formed the upper limit of the poorly developed nerve. Centrally, the lamina was widened due to an abnormal separation of its elements. Its uppermost fibers arched abruptly downward, especially on the temporal side, and were continued in the outer portion of the thick fibrous sheath which enveloped the poorly differentiated nerve below. Nasally, the laminated fibers turned outward, but less abruptly than temporally, and projected as finger-like processes into an intervaginal space (fig. 3). At some points these projections actually crossed the space and could be traced as far forward as the scleral promontory. Most of the fibers lay free in the space, however, and mingled with a meshwork of fibrillar tissue. The bulk of the middle and lower fibers deviated sharply forward into tissue, forming a sheath for the undifferentiated nerve. The exact termination of the lamina cribrosa could not be ascertained, but it appeared that the greater bulk arose from the region of the scleral promontory.

Nerve Sheaths: The intradural space about the malformed nerve was considerably wider than about the normal nerve above. The dural sheath on the temporal side was inclined outwardly; at the disk it formed an angle of 30 degrees with the nerve and bulged farther from the nerve as it continued backward. At the point of junction of the coloboma with the true nerve, it inclined nasally. On the nasal side, the dural sheath showed only a slight outward displacement.

The sheaths about the true nerve were normal in structure. At a point 2.5 mm. from the entrance of the nerve the arachnoid and the pia turned sharply outward and downward and merged with the dura. There was thus formed an artificial

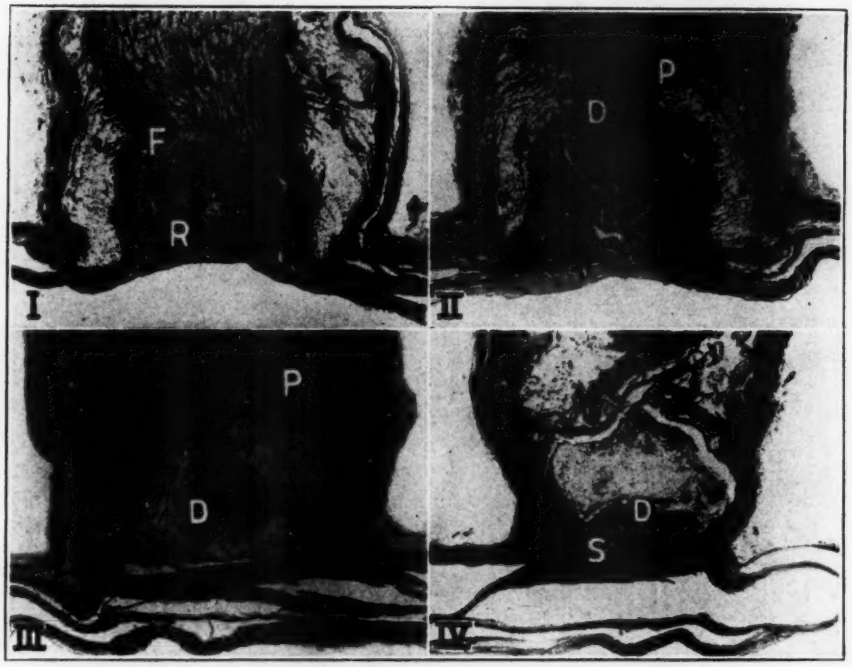

Fig. 7.—Section through the intermediate, upper and lower levels of the disk. (The levels are indicated in figure 8.) I is the intermediate level above or below the central hyaloid area (Van Gieson's stain). *F* indicates the nerve fibers in the undifferentiated nerve; *R*, the retinal vessels at the periphery of the nerve. II is the level near the edge of the disk. *P*, the pia of the normal nerve, and *D*, the dural sheath of the undifferentiated nerve, merge. Retinal vessels emerge at this level. III is the section at the edge of the disk. *D* indicates the sheath of the undifferentiated nerve surrounded by a meshwork of dural fibers containing blood vessels derived from the central retinal artery in the normal nerve, and *P*, the pia of the nerve above. IV is the section at the outer edge of the disk, indicating fusion of the dural meshwork, *D*, with the sclera at the margin of the disk, *S*.

or false vaginal space anterior to this point of junction. The outer edge of this space consisted of perceptibly thinned dura, while its inner side was made up of an irregular fibrous sheath which lined the undifferentiated nerve. This sheath resembled closely the outer dural sheath of the nerve. Its outer portion,

in addition to its fibrous structure, was rich in elastic fibers. The bulbar or anterior end of the space was formed by the union of the scleral promontory with the sheath of the undifferentiated nerve. This portion of the space was considerably wider nasally than temporally. The space itself was filled with a syncytium resembling areolar tissue but which in reality consisted of thin fibrocellular septums rich in capillaries, and which, on account of its elastic structure and its intimate connection with the outer dural sheath membrane, was undoubtedly

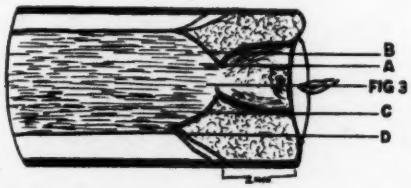

Fig. 8.—Diagram of the coloboma. *A, B, C* and *D,* respectively, indicate the levels at which sections I, II, III and IV in figure 7 are taken. The coloboma comprises a central undifferentiated nerve tissue containing remnants of the hyaloid system and a space surrounding it on all sides. In figure 3 this space is termed the "false intervaginal space."

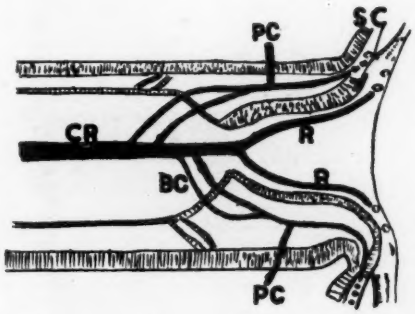

Fig. 9.—Diagram of the vascular supply of the undifferentiated nerve and surrounding space. *S* indicates the sclera; *C,* the choroid; *R,* the retina, and *CR,* the central retinal vessel in a normal nerve; *BC,* the branches of the central vessel, pierce the pial sheath and enter the space about the undifferentiated nerve and communicate with short posterior ciliary vessels, *PC.* These enter the choroid. Retinal vessels, *R,* occupy the periphery of the undifferentiated nerve and emerge into the retina at the edge of the disk.

dural tissue intermingled with fragments of the lamina cribrosa, torn from their dural attachment. Large blood vessels, each with a dura-like tissue about them, were also present in the spaces. These blood vessels communicated with the short posterior ciliary vessels which entered the artificial vaginal space through the dura. Anteriorly they communicated with the vessels of the circle of Zinn.

Macular Area: The temporal edge of the macula (artificially detached from the choroid) was normal except for disarrangement of Henle's layer. The nasal portion was thin, and its elements were irregularly arranged. The foveal region was represented by a clear space lined in front by the anterior limiting membrane. The cone layer, the pigment epithelium and the lamina vitrea were absent in the

macular region. Beginning at the temporal edge of the macula, the choroid was also maldeveloped. Only an occasional vessel was seen. Pigment cells were sparse, and the stroma was replaced, as it were, by an overdevelopment of the laminated fibers of the suprachoroidea which appeared to have replaced the choroid for the most part. Above and below the macular area the choroid was well developed and normal in all respects. Nasal to the fovea, the pigment layer of the retina reformed and near the edge of the optic canal became reduplicated and enveloped bundles of sclera-like tissue.

Peripapillary Zone: This area was distorted due to the enlargement of the optic canal, the interposition of a pseudovaginal space on either side and the presence of a separate dural sheath about the undifferentiated nerve. Temporally, the retina was fused with the thin undifferentiated choroid, and opposite the scleral promontory it was continuous with the dural sheath of the false nerve. Nasally, the retina was normal. The choroid was well formed and jutted forward and turned at right angles to join the sheath on this side. It thus formed the anterior boundary of the false vaginal space nasally.

COMMENT

The anomaly described was essentially a coloboma of the nerve at its entrance, the nerve being replaced by rudimentary retinal tissue. Associated with this defect were the persistence of remnants of the hyaloid system, widening of the scleral canal, dislocation of the lamina cribrosa and a choroidomacular coloboma.

It is possible, of course, to ascribe the presence of rudimentary nerve tissue to the ingrowth of primary retinal layers into the optic stalk. In the presence of this abnormal circumstance, persistence of the hyaloid system might well result. This explanation, in which the hyaloid system assumes a secondary rather than a primary rôle in the formation of the coloboma, would appear to be more attractive. What cannot be explained from the microscopic study, however, is the relation of the undifferentiated nerve to the widening of the optic canal and distortion of the associted structures, unless it is explained on the basis of disturbed growth relationship.

The inclination of the nerve nasally suggests that a detachment began on the temporal side, and a continuation of this mechanical force produced not only separation of the lamina cribrosa from its scleral attachments but a dehiscence of a portion of the dura as well. Only in this manner can one explain the dura-like sheath of the undifferentiated nerve. The interventing space thus produced would appear to consist of fragments of dura and lamina. However, whether this deviation of the nerve was a primary force or whether it ensued as a result of the outward displacement of the dura and widening of the optic canal cannot be definitely stated. The enlargement of the globe would follow on the weakening and consequent ectasia of the sclera at the edges of the canal.

ACUTE ALCOHOLIC AMAUROSIS

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AND
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Six cases of total but temporary blindness associated with acute poisoning due to ethyl alcohol have been observed by us during the past two years. Five of these were seen in the wards of the medical service of the psychiatric division of the Bellevue Hospital during the year ending Dec. 31, 1937. The history was that during or soon after the ingestion of alcoholic liquor the patient suddenly became blind. By the time these patients reached us, usually within a few hours, examination revealed total blindness in both eyes, normal pupillary reactions to light and convergence (as in the amaurosis associated with uremia) and normal fundi. Complete recovery, as a rule, followed within twenty-four hours; in 1 case, however, improvement was more gradual.

We believe that this condition develops with sufficient frequency to merit consideration whenever sudden blindness occurs in association with alcoholism. We are, therefore, presenting the findings in 4 typical cases.

REPORT OF CASES

CASE 1.—S. C., a 33 year old man, was admitted to the medical service of the psychiatric division of the Bellevue Hospital on Sept. 15, 1937, because of the sudden onset of total blindness twenty minutes before admission. His history included addiction to alcohol of at least ten years' duration. During the past six months he had been consuming about 1 quart of whisky daily and eating little. During the past year he had had four similar attacks of blindness, each of which cleared up completely and spontaneously within twenty-four hours. Shortly before the onset of the present attack of blindness he had taken several drinks of whisky.

On admission he was confused, disoriented, confabulating and totally blind. There was complete paralysis of all the extraocular muscles. The pupils were equal and reacted to light and convergence. The fundi were normal. The patient had pellagra, as manifested by the characteristic glossitis, stomatitis, dermatitis and diarrhea. There was no peripheral neuritis.

Within twelve hours the external ophthalmoplegia had disappeared, and vision had returned. Marked nystagmus was present by this time. During the following

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two days the patient became more severely ill. The picture of acute alcoholic encephalopathy with convulsions and paresis of both external rectus muscles with esotropia developed. Vision was 10/200 in each eye. During this period the patient had received a diet low in the pellagra-preventive factor. He was then given, in addition, 18 Gm. of vegex[1] by mouth and 10 mg. of synthetic crystalline vitamin B_1[2] by parenteral administration daily. Four days after the institution of this regimen the paresis of the external rectus muscles and the acute encephalopathic picture had disappeared; the glossitis, stomatitis and diarrhea had cleared, and the dermatitis was considerably improved. The patient continued to manifest a Korsakoff psychosis. Twelve days after admission the vision was 16/30 in the right eye and 16/40 in the left eye. Because of the psychosis it was not possible to test the visual fields satisfactorily.

Case 2.—L. S., a 35 year old taxi driver, was admitted to the medical service of the psychiatric division of the Bellevue Hospital on Dec. 11, 1937, because of the sudden onset of total blindness. His wife stated that two years previously he had been hospitalized for eight days because of an injury to the skull. One and one-half years previously he had been hospitalized again because of trauma to his arm and chest and perhaps to the head. He usually took alcohol only in moderation. At about 3 a. m. on the day of admission he began drinking "corn whisky." He had imbibed from 1 to 2 pints of this when, at 7:30 a. m., he stumbled over a chair, fell to the floor and realized that he was totally blind.

Examination when he was admitted showed a well developed, obese man, who did not appear ill but complained of headache and blindness. He was unable to perceive light. The right pupil was slightly larger than the left, but both were regular in outline and reacted promptly to light. There was a coarse bilateral nystagmus. Bilateral subconjunctival hemorrhages were present. The fundi were normal. There were no signs of peripheral neuritis. The blood pressure was 106 systolic and 76 diastolic. The patient was afebrile and clear mentally.

Analysis of a sample of the corn whisky consumed by the patient showed absence of methyl alcohol.

Two days after his admission there was perception of light in the right eye, but the left eye was still totally blind. His vision did not improve within the next eight days. Ten days after admission 50 mg. of thiamin (crystalline vitamin B_1)[2] was administered once daily by intravenous injection. This was continued until a total of 350 mg. was given. Three days after the institution of this therapy the patient was able to discern moving objects with the right eye; five days later vision in the right eye was 20/15, and the visual field was normal. The left eye was first able to see light seventeen days after the onset of the amaurosis; two days later vision in that eye was limited to counting fingers at 1 foot (30 cm.). The vision in the left eye remained the same for five days, and then the patient claimed that the eye was totally blind. The vision in this eye continued to be nil for two weeks. During this time the patient was having many financial worries. All tests for hysterical amblyopia gave negative results, but the pupils were equal in size and reacted to direct and consensual light equally. He complained of headaches radiating from the frontal to the occipital region and said that they were severe in the latter region. At the end of two weeks, while the examiner was testing the patient with complementary colors in another effort to detect hysterical amblyopia in the left eye, the patient admitted

1. The vegex was supplied by Vegex, Inc.
2. The vitamin B_1 was supplied by Merck & Co.

seeing very blurred objects. At that moment he was told that he would rapidly recover his vision. A solution of silver nitrate strong enough to produce pain was applied to the lids of the left eye. The vision became 20/70 in ten minutes. In thirty minutes it was 20/40, and the visual field was normal. The patient stated that vision in the left eye had never been as good as that in the right, but on the following day it was 20/30. He has retained vision of 20/15 in the right eye and of 20/30 in the left eye.

CASE 3.—L. N., a 39 year old white man, was admitted to the medical service of the psychiatric division of the Bellevue Hospital on the night of Dec. 15, 1937, because of the sudden onset of total blindness four hours prior to admission. The history was that at about 4 p. m. he had drunk three or four bottles of beer with his supper. While playing with his children after supper "something snapped," and he became totally blind. He was brought to the hospital in an ambulance. He had never had a similar attack, but three days previously he had noticed that his eyes watered and that his vision was slightly blurred when he tried to read.

He had a chancre in 1918, which was treated by cautery alone, meningitis in 1936 and frequent traumatic injuries to his head, none of which was so serious as to necessitate hospitalization. He was employed as a sheet metal worker for many years and recently had been doing a great deal of soldering in a poorly ventilated room. He and his fellow workers were often forced to take rest periods because of the irritating fumes, but he had never heard of attacks of blindness in any of the other employees. He admitted that it was his habit to drink three or four bottles of beer daily with his evening meal, but no further history indicative of addiction to alcohol could be elicited. He was supported in this history by his wife. Two weeks after he was discharged, however, he presented himself for examination because of pain in his chest. He then appeared to be acutely intoxicated, and he admitted imbibing 2 jiggers of gin before coming to the clinic. He again stated that he was not addicted to the use of alcohol.

When admitted to the hospital on December 15 he appeared well developed and well nourished and not acutely or chronically ill. He was totally blind. The right pupil was larger than the left; both were regular and reacted promptly to light. There was no palsy of the extraocular muscles and no nystagmus. Ophthalmoscopic examination showed a normal fundus. There was an indentation in his forehead caused by an old injury. All the superficial and deep reflexes were intact, and there were no abnormal reflexes. The was no evidence of peripheral neuritis. The blood pressure was 130 systolic and 90 diastolic, the pulse rate was 80, and the temperature was normal. The patient was clear mentally.

The following morning, December 16, he stated that he had awakened at about 4 a. m. and found his vision to be normal (about twelve hours after the onset of blindness). Examination at 10 a. m. revealed vision of 20/20 in each eye. The optic disks and the fundi were normal. The right pupil was larger than the left, but both reacted to light and in convergence. The visual fields were found to be normal, and there were no scotomas. At no time did the patient show any other neurologic abnormalities or encephalopathic manifestations.

Analysis of the urine failed to reveal the presence of lead. Examination of the stained blood smear revealed no stippling or other abnormalities. The Wassermann reactions of the blood and spinal fluid were negative, and the colloidal gold curve of the spinal fluid was normal. The vision has remained normal.

CASE 4.—J. B., a 30 year old Jewish man, was brought to the Institute of Ophthalmology of the Columbia Presbyterian Medical Center on April 5, 1936, totally blind and mildly intoxicated. He had been addicted to the use of alcohol

for at least ten years, consuming an average of from 1 to 2 pints of whisky daily. His parents had hospitalized him in various institutions for the treatment of alcohol addiction, without effect. The history as obtained from the patient and his parents was that he had drunk about 2 quarts of whisky during the preceding two days. His father then confined him to a locked room to prevent him from drinking. The patient, however, found some "Whiz," an antifreeze mixture for automobile radiators, in a closet of the room and drank a quart of this as well as 10 cc. of perfume. Two hours later he became totally blind. He had no headache and did not vomit but acted intoxicated. An oculist who was consulted told the family that the patient would never see again. Eight hours after the consumption of the "Whiz" he entered the hospital.

Examination revealed a hematoma behind the left ear, the result of a fist fight on the previous day. Both lids of the right eye showed marked ecchymosis due to a fall against a bedpost that day. Vision was nil in each eye, but the pupils were round, about 3 to 4 mm. in size, and reacted promptly to light and in convergence. The possibility of hysteria or malingering was considered. The patient's answers and actions at all times, however, were consistent with those of a man totally blind. He failed to blink when an object was suddenly passed in front of his eyes; he blundered into a wall when permitted to walk unaided; he pointed toward the examiner when asked where the latter was in the room, because he could tell from what direction the voice came.

An infusion of saline solution was given, and sedatives were administered because of his great anxiety over his blindness. Inhalations of carbon dioxide and oxygen were given for ten minutes every four hours, and fluid intake was forced. Twelve hours after entering the hospital the patient had perception of light in each eye; three hours later he could see large objects, and in another three hours the vision was 20/15 in each eye, and the fields of vision were normal.

Analysis of the antifreeze mixture left in the bottle from which the patient had drunk showed that it consisted of from 50 to 60 per cent ethyl alcohol, water and small traces of a denaturing agent, pyridine. Methyl alcohol was not found by chemical examination. The manufacturer of the antifreeze mixture confirmed that it contained no methyl alcohol as then made. Analysis of the perfume, also, revealed absence of methyl alcohol.

At the urgent request of the patient's parents he was told that if he ever drank again he would become blind, and this was emphasized on several occasions. Three weeks after his recovery from the sudden amaurosis he returned, stating that his vision had rapidly failed in the past few hours. He denied that he had been drinking. The vision was approximately 20/200 in each eye, but with encouragement this improved to 20/30 in a few minutes. He finally admitted drinking whisky. The amblyopia was apparently of the hysterical type. The following morning his vision was 20/15. For the past two years the patient has had no further ocular complaints.

Two additional patients with acute alcoholic amaurosis have been seen in the medical service of the psychiatric division of the Bellevue Hospital within the past year. The cases are not reported as they are similar to case 3. In these patients, too, there was total blindness, with active pupils, normal fundi and spontaneous recovery within twelve hours.

COMMENT

In an analysis of 8,800 specimens of illicit liquor, reported by Lythgoe [3] in 1928, only 8 were found to contain methyl alcohol. In a similar analysis of 100 specimens of illicit liquor, Hunt [4] found that only 6 contained small amounts of methyl alcohol. He stated: "The often expressed fear of injury to the eyes from such small percentages of methyl alcohol is probably not well founded. To get even 15 cc. of methyl alcohol in the samples tested in this study would involve the taking of a surely fatal dose of ethyl alcohol." Hunt concluded that the only poisonous substance of significance in the samples examined by him was ethyl alcohol. Another point of interest was his finding that a sample of genuine bottled-in-bond whisky was slightly more toxic than all but three of the samples of illicit liquor, in which the slightly higher toxicity was due to the higher content of ethyl alcohol. Harger,[5] also, concluded that the poison in "poison liquor" is usually ethyl alcohol.

During 1937 9,667 persons were admitted to the psychiatric division of the Bellevue Hospital because of alcoholism. Only 2 suffered from methyl alcohol poisoning; both patients had attempted suicide, and had recovered from the effects of the acute poisoning due to the methyl alcohol within twenty-four hours. Neither patient showed any residual pathologic process or any immediate or delayed impairment of vision. Chemical examination of the liquors consumed by our patients with amaurosis was made in the 2 instances in which a sample could be obtained. Both samples showed nothing significant except ethyl alcohol. Methyl alcohol was definitely not present. In 1 other instance the beverage imbibed was of a nationally advertised and widely consumed brand.

From the foregoing facts, it would appear that methyl alcohol poisoning among persons addicted to alcohol is rare and that amaurosis due to methyl alcohol poisoning is a still greater rarity. Temporary total blindness, however, occurred in 0.05 per cent (5 of 9,665) of instances of ethyl alcohol poisoning. The incidence may actually have been considerably larger, as many of these patients, owing to the transient nature of the blindness, were probably not seen by the physician while blind, and their history is not recorded.

That ethyl alcohol poisoning may cause temporary total blindness has not been generally recognized. De Schweinitz [6] made the following

3. Lythgoe, H. C.: Character of Illicit Liquor upon Massachusetts Market, New England J. Med. **198**:228 (March 22) 1928.

4. Hunt, R.: An Examination of the Toxicity of One Hundred Samples of Illicit Liquor, New England J. Med. **198**:230 (March 22) 1928.

5. Harger, R. N.: What Is the Poison in Poison Liquor? J. Indiana M. A. **23**:137 (March 15) 1930.

6. de Schweinitz, G. E.: The Toxic Amblyopias: Their Classification, History, Symptoms, Pathology, and Treatment, Philadelphia, Lea Brothers & Co., 1896, p. 26.

statement: "Now and then acute alcoholism seems to have been responsible for almost complete blindness without ophthalmoscopic change, rapidly disappearing under antiphlogistic treatment and total abstinence." He referred to 1 such instance.

Strader [7] in 1927 reported a case which may represent another instance of acute amaurosis associated with ethyl alcohol poisoning.

> A man 24 years of age began drinking "moonshine" at about 2:30 p. m. on Oct. 9, 1926. He had imbibed about 1½ pints by 11 p. m., when he noticed that his vision was failing. Four hours later he was completely blind. He was first seen at 9:30 a. m. on October 10. His vision was reduced to perception of light in each eye. There was moderate congestion of the retinal vessels; otherwise the fundi were normal. He complained of supraorbital headache and was treated by lumbar puncture. By October 12 he was able to count fingers at 6 inches (15 cm.), and one week after the onset his vision was 20/20 in the right eye and 20/20 in the left eye with a —0.50 cyl., axis 90, with normal visual fields and no scotoma. He was seen again on November 29, at which time there was no change in vision or in the fundi.

Strader stated in his report that he assumed that the "moonshine" probably contained methyl alcohol. From the facts cited concerning the toxicity of illicit liquors and because of the resemblance of this case to those observed by us, it is not unlikely that the amaurosis was due to acute poisoning with ethyl alcohol.

The nature or location of the lesion responsible for the transient blindness in these patients cannot be described with any degree of certainty. We believe, however, that the location is most likely central and that it may be classified in that protean and loosely defined group of disease complexes collectively described as "alcoholic encephalopathy."

While hysterical amblyopia subsequently developed in 2 of our patients, we do not believe that this was the initial responsible factor in any of our cases. In the cases reported the onset of blindness occurred while the patients were suffering from acute alcoholic intoxication. Apparently acute poisoning with ethyl alcohol is necessary for the development of this disease. We believe, however, that a background of addiction to alcohol is probably a prerequisite. It is of interest also to note that in all of our cases there was a previous history of trauma to the head. The poor tolerance of ethyl alcohol shown by persons who have had injuries of the skull is well known.

All our subjects recovered, the only constant factor in their therapy being the withdrawal of alcohol. We believe that the therapeutic measures employed in these subjects probably in no way influenced the outcome and that recovery is spontaneous in this disease.

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7. Strader, G. L.: Toxic Amblyopia from Drinking, Am. J. Ophth. **10**:359 (May) 1927.

SUMMARY AND CONCLUSIONS

We have reported 4 cases of acute alcoholic amaurosis, characterized by total blindness in both eyes, normal pupillary reactions to light and convergence, normal fundi and rapid improvement. We have presented evidence and discussed our reasons for considering this disease a manifestation of acute poisoning with ethyl alcohol. We have pointed out that methyl alcohol poisoning among persons addicted to the use of alcohol appears to be of rare occurrence.

In conclusion, we believe that acute alcoholic amaurosis, although a disease of infrequent occurrence, demands a correct etiologic diagnosis because of the excellent prognosis which can be offered in this disease as compared with the poor prognosis which is generally given in the cases of blindness due to methyl alcohol poisoning.

PANOPHTHALMITIS AND SYMPATHETIC OPHTHALMIA

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It is an old saying that once in a while panophthalmitis leads to sympathetic ophthalmia, whether or not the injured globe has been eviscerated. This is the reason why in Vienna evisceration has been given up, and whenever it is necessary to incise a panophthalmic globe it is customary later to excise the stump. In textbooks it is almost classic to state that in panophthalmitis the purulent process destroys the entire uveal tract and leaves no place for the development of sympathetic ophthalmia. So convinced were the older ophthalmologists of the efficacy of purulent inflammation that, taking the hint from farriers, they introduced setons into injured eyes to produce pus as a prophylactic measure. It is common knowledge in the laboratory that in practically every phthisic globe more or less of the ciliary body and the choroid and also those extensions which the uvea sends into the emissaria of the sclera remain. Apparently the extensive, but at the same time never complete, destruction of the uveal tract is not the sole cause of the degree of protection supposed to be offered by panophthalmitis.

The pathogenesis of sympathetic ophthalmitis has served for decades as a favorite field of speculative research. Most of the known facts concerning this disease are explained by the assumption that the exciting agent is a virus which enters the eye by way of the wound, where it produces the so-called "inoculation chancre" of Redslob, from which it spreads to other parts of the uvea of the same eye and from thence by way of the blood stream to the uvea of the fellow eye. In a panophthalmitic eye it is believed that the virus may live in a state of symbiosis in combination with whatever germ may be the cause of the purulence.

EXPLANATION OF VARYING AMOUNTS OF UVEA REMAINING IN PHTHISIC GLOBES FOLLOWING PANOPHTHALMITIS

Closed Panophthalmitis.—In cases in which the opening in the cornea or sclera is small, the purulent process within the globe goes on under high pressure, destroying in succession the retina

Read at the Seventy-Fourth Annual Meeting of the American Ophthalmological Society, San Francisco, June 9, 1938.

and the choroid, the latter almost never entirely. The sclera finally becomes infected, and being distended by the high intraocular pressure, ruptures at the wound or at the equator. It would seem that the longer the perforation was delayed, the more thorough would be the destruction of the uveal tract. It may be argued that the less uvea left, the less likelihood there is of sympathetic infection. Furthermore, whatever uvea is spared may be so damaged by toxins and high pressure that the virus may not find it a favorable medium for propagation. Closed panophthalmitis is no less a clinical than a pathologic entity. It may manifest itself within twenty-four hours after the injury. The excruciating pain increases with the increase in intraocular pressure. The edema of the bulbar conjunctiva and the protrusion and immobility of the globe indicate scleral and orbital involvement. With the reduction of pressure by incision or spontaneous rupture, the pain promptly abates.

Open Panophthalmitis.—In cases in which the opening in the cornea or sclera is large, the formation of pus goes on under no great pressure, and consequently abscesses and necroses in the choroid are likely to be less extensive, much of the toxins being eliminated through the wide opening. The sclera in cases of open panophthalmitis is usually little affected, so that protrusion and immobility are not prominent clinical features.

More of the uveal tract is saved in the open than in the closed type of panophthalmitis, so that of the two types one would consider the open type to be the more dangerous. Under this classification come also cases in which the eyes have gone on to phthisis after destruction of the cornea due to a serpiginous or gonorrheal ulcer, the opening thus brought about having the same effect as a perforating wound.

To be sure the kind of germ that produces the pus and the degree of toxicity come into consideration in accounting for the destruction of the uvea, but the greatest role perhaps is that played by the size of the wound; that is, the extent of destruction of the uvea depends on whether an "open" or a "closed" type of panophthalmitis is present.

INCIDENCE OF PANOPHTHALMITIS IN SYMPATHETIC OPHTHALMIA

Panophthalmitis is of relatively rare occurrence today, not only because severely injured eyes are excised before the infection is far advanced but because the usual infecting germs do not lead to a widespread purulence. However, in regions with warm climates, such as Egypt, panophthalmitis is still relatively frequent, whereas in the United States it probably represents not more than 2 or 3 per cent of all intraocular infections following injuries.

In regard to the incidence of panophthalmitis in cases of sympathetic ophthalmitis, one may glean an idea from the fact that of 101 globes showing characteristic sympathetic tissue, reported in a previous paper,[1] there were only 3 which had been affected with panophthalmitis. In this same material there were 9 instances of typical sympathetic infiltration of the choroid without involvement of the fellow eye. Of these 9, 7 followed common endophthalmitis and 2 followed panophthalmitis. Thus 3 cases of panophthalmitis in a series of 101 cases of sympathetic ophthalmia, that is about 3 per cent, is surely not an

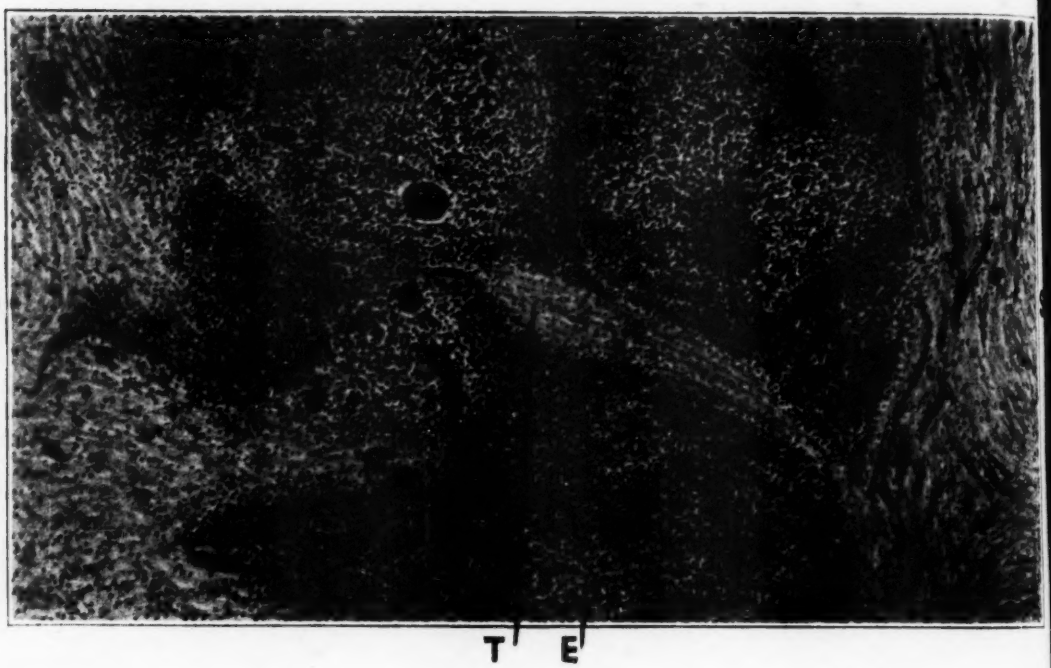

Fig. 1.—Section of a phthisic globe of a boy aged 14 years with sympathetic ophthalmitis. The cornea was perforated with a knife and the lens extruded. Typical sympathetic nodules were seen in the ciliary body. The section from the choroid is not well outlined because of the panophthalmitis. A large number of nests of epithelioid cells (*E*) lie in the midst of a dense lymphocytic infiltration. Along the internal surface granulation tissue (*G*) mingles with the specific infiltration of the choroid. Along the external surface the sclera (*S*) is inflamed. Extending from the sclera into the specific infiltration, there is a long band of connective tissue (*T*) caused by panophthalmitis.

insignificant figure; this suggests that a panophthalmitic eye may not be so harmless as has been commonly thought.

1. Samuels, B.: Significance of Specific Infiltration at the Site of Injury in Sympathetic Ophthalmia, Arch. Ophth. **9**:540 (April) 1933.

DIAGNOSIS OF SYMPATHETIC TISSUE IN PANOPHTHALMITIS

The diagnosis of sympathetic tissue in a phthisic globe following panophthalmitis is beset with difficulties, principally because of the damage done to the choroid by its having participated in the purulent inflammation.

To demonstrate difficulties of diagnosing sympathetic ophthalmia in panophthalmitic globes, the following 2 cases are reported:

CASE 1.—*Open panophthalmitis.*

A patient aged 66 had spontaneous iridocyclitis with an increase in tension; later an ulcer of the cornea developed, with perforation, followed by panophthalmitis.

The cornea was not included in the preparation examined microscopically. The iris and ciliary processes were destroyed. The choroid was widely detached and was enormously thickened. The retina was necrotic. No perforation of the sclera was found, and neither should one have been expected in accordance with the history of destruction of the cornea. A wide detachment of the choroid indicated that some of the contents of the globe had been expelled through the corneal defect, thus accounting for the missing lens.

The stumbling block encountered in the study of this phthisic globe lay in the presence of irregular islands of a reddish color in the midst of a dark blue background of densely packed lymphocytes in a greatly thickened choroid. These islands gave the impression of being islands of epithelioid cells, such as are common in sympathetic ophthalmitis, under which heading the microscopic section was originally filed. In reality, an enormous mass of granulation tissue was being dealt with. What was so peculiar was its presence in the choroid, where granulation tissue is seldom found, and its great extent. This was made possible by the natural looseness of the choroidal stroma allowing a large abscess to develop which organized into granulation tissue. A factor contributing to the expansion of the choroid as the abscess developed was doubtlessly the low intraocular pressure of a panophthalmitic eye. The organized mass contained few pus cells in comparison with a vast quantity of lymphocytes. Above all else, there were numerous distended capillaries and solid endothelial buds. These succulent looking vascular elements, taking a reddish stain and occurring in groups, so simulated islands of epithelioid cells as to raise the question of sympathetic ophthalmitis.

In this connection it was recalled that sympathetic tissue is composed mainly of two kinds of cells, namely, lymphocytes and epithelioid cells, with or without giant cells. All other cells, such as plasma cells and eosinophils, are merely accidental, being an expression of another disease, for it should be remembered that sympathetic ophthalmitis is always combined with some other condition. Furthermore, sympathetic tissue, like tuberculous tissue, is remarkable for the sparsity of its blood vessels.

Finally, the granulation showed an unusually small number of fibroblasts, in spite of its great vascularity. In explanation, it may be that with so many blood vessels of all sizes to spring from, endothelial buds and capillaries came into being before there was time for fibroblasts to develop.

CASE 2.—*Open panophthalmitis.*

A boy aged 14 years two weeks before enucleation of his eye received a stab in the eye from a knife, causing prolapse of the iris, which was excised. Panophthalmitis developed from the infected wound.

Microscopic examination showed the iris to be heavily inflamed, but there were no typical changes. The ciliary body contained numerous pus cells and a number of plasma cells. The appearance of the choroid was so similar to that in case 1 that it came in the same category. The choroid was thickened, and small reddish islands were observed standing out against a bluish background. However, under high magnification the choroid was found to be packed with plasma cells, with relatively few lymphocytes, and the reddish islands turned out to be capillaries and solid endothelial buds. The reaction, as in the former case, was excited directly by toxins from the infected area in the vitreous cavity.

It is interesting that the predominant cells in the granulation tissue in case 1 were lymphocytes and in case 2 plasma cells. Indeed, the almost solid array of plasma cells in case 2 told at once that the condition was not sympathetic ophthalmitis, for however numerous plasma cells may be in sympathetic tissue they never predominate, and the same is true for eosinophils.

CLINICAL IMPORTANCE OF DIAGNOSIS OF SYMPATHETIC OPHTHALMITIS FROM MICROSCOPIC PICTURE

Clinically, the diagnosis of sympathetic ophthalmitis on the basis of microscopic observations plays an important role because it is not always possible to ascertain whether an iritis in the uninjured eye is a genuine sympathetic ophthalmitis or is due to syphilitic or tuberculous iridocyclitis. It is well known that the clinical picture of these types of iridocyclitis often differs but little from that of sympathetic ophthalmitis. The only way to clear this up beyond dispute is to excise the injured blind eye and examine it microscopically. The diagnosis of sympathetic ophthalmitis is of special importance from the standpoint of treatment. In the treatment of ordinary iridocyclitis comparatively mild remedies are usually employed, but in the treatment of sympathetic inflammation the measures may be heroic; for example, when the patient is young and vigorous the malarial cure may be advised. Much may depend on the report from the laboratory.

ORDINARY LYMPHOCYTIC INFILTRATION AND SYMPATHETIC LYMPHOCYTIC INFILTRATION IN THE CHOROID

In the usual cases of perforation complicated by infection in the vitreous the choroid is so well protected from toxins by the retina that

it does not participate in the reaction. There are, however, exceptions to this rule, in which toxins in the vitreous travel to the choroid by a roundabout route. These exceptions follow:

1. When the infection in the vitreous is severe, the toxins diffuse into the papilla and from thence into the choroid, setting up a narrow circumpapillary zone of infiltration composed purely of lymphocytes, because the toxins arrive in a diluted state. The retina seems to offer a greater resistance to the transfusion of toxins than the papilla, although

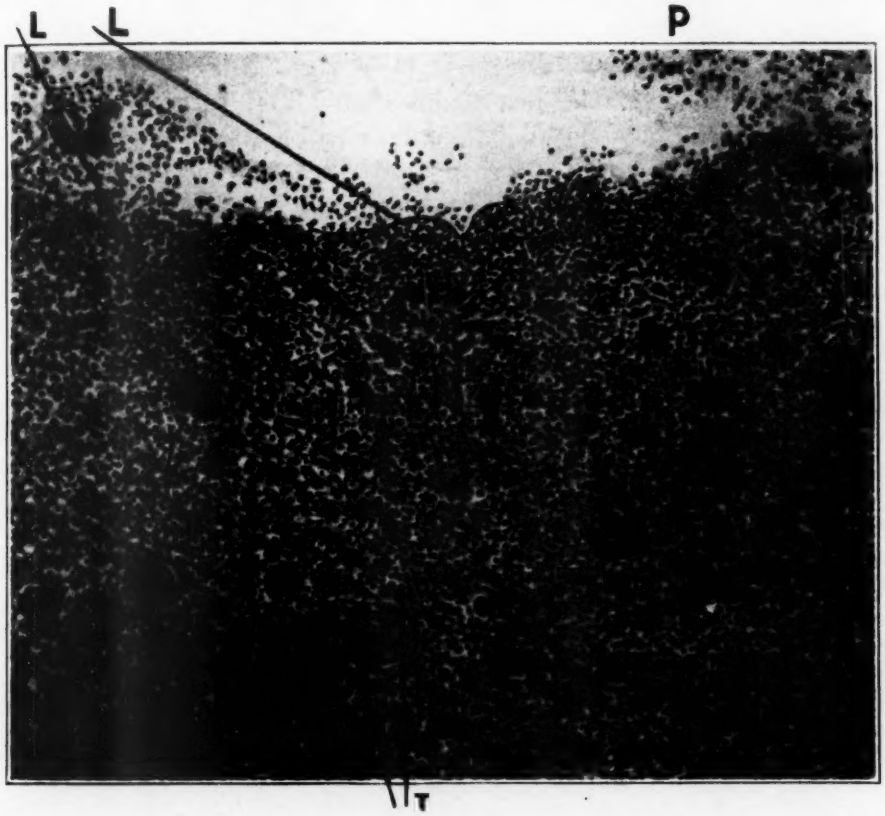

Fig. 2 (case 2).—Section from a phthisic globe with granulation tissue in the choroid, simulating sypmpathetic tissue following panophthalmitis. The choroid can be identified by the presence of a number of wavy remnants of the lamina vitrea (*L*). Above these is the subretinal space, filled with an albuminous fluid containing pus cells (*P*). The thickness of the choroid is greatly increased by the presence of typical granulation tissue. A large number of distended and engorged blood vessels stand out prominently. Scattered about are many irregularly outlined islands of solid vascular endothelial buds simulating islands (*I*) of epithelioid cells characteristic of sympathetic ophthalmitis. A great quantity of lymphocytes with relatively few leukocytes is distributed in the granulation tissue, adding to the similarity with sympathetic tissue.

the tissue of the papilla is much thicker. Apparently a more active exchange of fluid goes on between papilla and choroid within the choroidal canal than between the general layout of retina and choroid. It is true the outer layers of the retina are nourished by the choriocapillaris, and there must be an active exchange of fluid between the tissues, yet a kind of barrier has to be supposed to exist between the inner and the outer layers of the retina along the line where the area of the retinal system of blood vessels touches the domain of the choroidal system. Whatever this barrier is, apparently it is more effective than the lamina vitrea, which is interposed between the choriocapillaris and the retina.

2. At the same time that toxins may diffuse backward from an infection in the vitreous they may also diffuse forward, producing a reaction in the flat part of the ciliary body, and from thence they diffuse into the choroid, producing a circumscribed lymphocytic infiltration of the choroid at the ora serrata analogous to the circumpapillary infitration.

3. Whenever the choroid is directly injured through the retina, as by an intraocular foreign body, it is just at the place of impact that a lymphocytic infiltration takes place. Such a reaction gradually abates. This localized lymphocytic infiltration can be readily recognized as an irritation caused by direct injury or secondarily by toxins diffused from the vitreous by way of the damaged retina.

Of paramount importance in deciding whether or not a case of endophthalmitis or panophthalmitis is accompanied by sympathetic infiltration is a study of the condition of the retina. To reiterate, when the retina is intact the choroid should be practically free of reaction in ordinary endophthalmitis, with the three exceptions mentioned. Lymphocytic foci scattered here and there in the choroid under an intact retina, whether the retina is detached or not, after a perforating wound suggest at once the initial stage of sympathetic ophthalmitis, particularly if the cells are typically distributed along the walls of the larger veins. The picture is clearcut, the infiltrated choroid being bounded by an intact retina on the one side and an intact sclera on the other. In comparison, when the retina is destroyed and granulation tissue in the vitreous space mingles with granulation tissue in the choroid or even with genuine sympathetic infiltration, the picture is complicated and calls for special interpretation.

CONCERNING EXPERIMENTAL WORK IN SYMPATHETIC OPHTHALMITIS

Although it may seem a digression from the main subject, I should like to point out some bearing that the material in this paper may have on experimental work in sympathetic ophthalmia that is done on ani-

mals. Infiltrations in the choroid of rabbits have been reported in which after injections of all kinds of substances into the vitreous cavity, including the virus of herpes simplex, the reaction found has been considered almost if not exactly identical with that of sympathetic ophthalmitis in human beings. However, the necrosing effect that these injections may have on the delicate retina seems to have been widely disregarded. There never can be any ground for discussion as to a similarity to sympathetic ophthalmitis if after an injection into the vitreous of a rabbit the retina becomes necrotic, because an infiltration so produced has an absolutely different meaning from that of sympathetic ophthalmitis. It belongs to the realm of panophthalmitis and is the result of a toxic influence directly exerted on the choroid.

Adding more difficulty to a statement regarding the relationship of the condition produced experimentally to symphatic ophthalmitis is the fact that it is almost impossible by any form of irritation to cause pus cells to be poured out in a rabbit's choroid. Only lymphocytes appear, probably because the choroid of a rabbit is constitutionally more resistant and the circulation more active in carrying away toxins than is the human choroid. Consequently, when a heavy lymphocytic infiltration is present in which groups of capillaries and endothelial buds may imitate nests of epithelioid cells, one may be tempted to make a wrong diagnosis of sympathetic ophthalmitis.

EXPERIMENTAL HYPERTENSION

VIII. VASCULAR CHANGES IN THE EYES

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AND

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In healthy dogs and monkeys (macaques) persistent elevation of the systolic and the diastolic pressure, with or without a decrease of renal excretory function, followed permanent partial constriction of the main renal arteries.[1]

The eyes of these hypertensive animals have been studied during a period of more than five years. A preliminary report [2] and an interim report [3] have been made.

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Read before the Section on Ophthalmology at the Eighty-Ninth Annual Session of the American Medical Association, San Francisco, June 16, 1938.

This study was supported by the Beaumont-Richman-Kohn Fund, and by special grants-in-aid from the Josiah Macy Jr. Foundation and Mr. N. L. Dauby, Mr. Alex S. Winter and associates, Cleveland.

1. (*a*) Goldblatt, H.; Lynch, J.; Hanzal, R. F., and Summerville, W. W.: Experimental Hypertension Due to Renal Ischemia, Bull. Acad. Med. Cleveland **16**:6, 1932; (*b*) Studies on Experimental Hypertension: I. The Production of Persistent Elevation of Systolic Blood Pressure by Means of Renal Ischemia, J. Exper. Med. **59**:347, 1934. (*c*) Goldblatt, H.; Gross, J., and Hanzal, R. F.: Studies on Experimental Hypertension: II. The Effect of Resection of Splanchnic Nerves on Experimental Renal Hypertension, ibid. **65**:233, 1937. (*d*) Goldblatt, H.: Studies on Experimental Hypertension: III. The Production of Persistent Hypertension in Monkeys (Macaque) by Renal Ischemia, ibid. **65**:671, 1937; (*e*) Studies on Experimental Hypertension: V. The Pathogenesis of Experimental Hypertension Due to Renal Ischemia, Ann. Int. Med. **11**:69, 1937. (*f*) Goldblatt, H., and Wartman, W. B.: Studies on Experimental Hypertension: VI. The Effect of Section of Anterior Spinal Nerve Roots on Experimental Hypertension Due to Renal Ischemia, J. Exper. Med. **66**:527, 1937. (*g*) Goldblatt, H.: Studies on Experimental Hypertension: VII. The Production of the Malignant Phase of Hypertension, ibid. **67**:809, 1938; (*h*) Experimental Hypertension Induced by Renal Ischemia, in Harvey Lectures, 1937-1938, Baltimore, Williams & Wilkins Company, 1938, p. 237.

2. Keyes, J. E. L., and Goldblatt, H.: Experimental Hypertension: IV. Clinical and Pathologic Studies of the Eyes; a Preliminary Report, Arch. Ophth. **17**:1040 (June) 1937.

3. Keyes, J. E. L., and Goldblatt, H.: Experimental Hypertension: Studies of the Eyes; Interim Report, Tr. Internat. Ophth. Cong., 1937, to be published.

These dogs exhibited two definite types of hypertension: a benign phase, without a decrease of renal excretory function, and an acute malignant phase, with very high blood pressure and severe damage of the renal excretory function. These two phases correspond to the benign and malignant phases of essential hypertension in man. The acute malignant phase of hypertension occurred, or was produced, in dogs already hypertensive, owing to constriction of the main renal arteries when the arteries were reconstricted to a great degree, or in healthy dogs in which the main renal arteries were markedly constricted from the beginning.

The group with benign hypertension without a decrease of renal excretory function (by far the larger), after a variable period, showed two types of clinical ocular change: A small number showed early retinal hemorrhages and edema, with early moderate and late severe retinal vascular disease. A larger number showed slowly progressive retinal vascular disease with an occasional small retinal hemorrhage and, more rarely, small areas of retinal edema. None of these showed papilledema (figs. 1 to 5).

Visible changes in the eyes of benign hypertensive animals were a late manifestation. The earliest and only constant change noted ophthalmoscopically in these dogs was usually an increase in the tortuosity of the retinal arteries. Owing to an anteroposterior, as well as a lateral, tortuosity of these arteries, the light reflex became interrupted, and the vessels presented a mottled appearance. In the monkey tortuosity of the arteries has not been much in evidence. Increase in the intensity and width of the arterial light reflex was, however, an early and persistent sign. Lessening of the caliber of the arteries was easily noticed in the monkey. In the dog, owing to the relatively small size of the retinal arteries, many of which are of the cilioretinal type, small variations in caliber were difficult to visualize. Common to the eyes of the two animals was the occurrence of localized retinal hemorrhages and areas of retinal edema. In the monkey, coincident with or succeeding these changes, increasing evidence of arterial disease was observed. The arteries and arterioles became narrower, the light reflex became wider and more brilliant, and gradually many vessels assumed a copper tint. Several small terminal arterioles resembled silver streaks. Vascular tortuosity and irregularity of outline were noticeably absent. In none of the animals have the retinal veins appeared diseased. In the eyes of hypertensive dogs no arteries resembling straight copper or silver wires or threads have been observed. Other changes seen in the eyes of the dogs have been preretinal, superficial and deep retinal hemorrhages, localized and general edema and detachment of the retina, perivasculitis,

Explanation of Color Plate

Fig. 1 (dog 3-8 R).—Drawing of the fundus of a hypertensive dog, three years after the blood pressure became elevated. Attention is directed to scattered hemorrhages, detachment of the retina and the white perivascular covering on the arterioles. A description of the eyes of this animal has been published.[2]

Fig. 2 (dog 5-9 R).—Drawing of the fundus of hypertensive dog, nearly five years after the final constriction of the renal arteries. Extensive periarteritis was present. Bilateral section of the thoracic portion of the splanchnic nerves and the lower four dorsal sympathetic ganglions was performed four years after the systolic blood pressure became elevated. After this operation the blood pressure remained at its previous high level. The animal lived more than five years after hypertension was established.

Fig. 3 (dog 2-10 R).—Drawing of the fundus oculi of a dog with benign hypertension of great degree and of thirty-four months' duration. The brown area is a scar following a previous hemorrhage. Both main renal arteries were successively greatly constricted. The systolic blood pressure rapidly became elevated and is usually in the neighborhood of 300 mm. of mercury. Bilateral section of the intrathoracic portion of the splanchnic nerves and the lower four thoracic sympathetic ganglions was without permanent influence on the blood pressure. At the time of writing the dog is still alive.

Fig. 4 (dog 2-35).—Drawing of the fundus of the right eye. Brown scars on the tapetum followed retinal hemorrhages. An arteriole on the temporal side of the nerve head had had a perivascular sheath of increasing density for twenty-six months. A gray haze had developed in the retina over diseased nasal arteries. At the time of writing the dog is alive and has a systolic blood pressure in the neighborhood of 230 mm. of mercury. After bilateral section of the splanchnic nerves and the lower four thoracic sympathetic ganglions, both main renal arteries were successively constricted. A moderate persistent elevation of systolic blood pressure ensued. A year later laminectomy was performed, and the anterior nerve roots, from the tenth dorsal to the second lumbar inclusive, were severed. There was a temporary lowering of blood pressure, which soon returned to the previous high level.

Fig. 5 (dog 2-50 L. 46).—Microscopic drawing of a choroidal arteriole. A portion of the wall is necrotic. There are a dissecting hemorrhage through the wall and extravascular hemorrhage.

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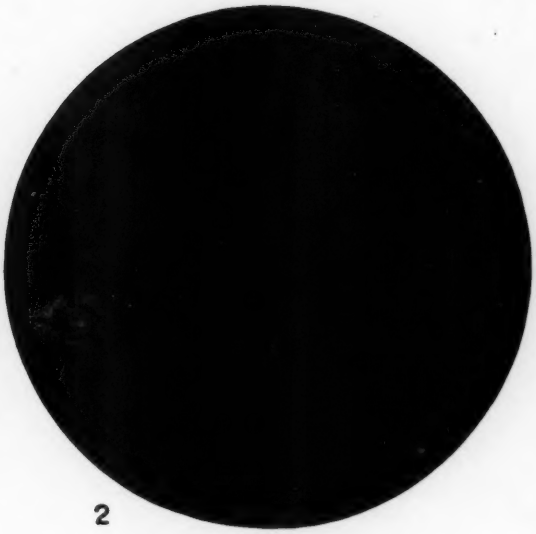

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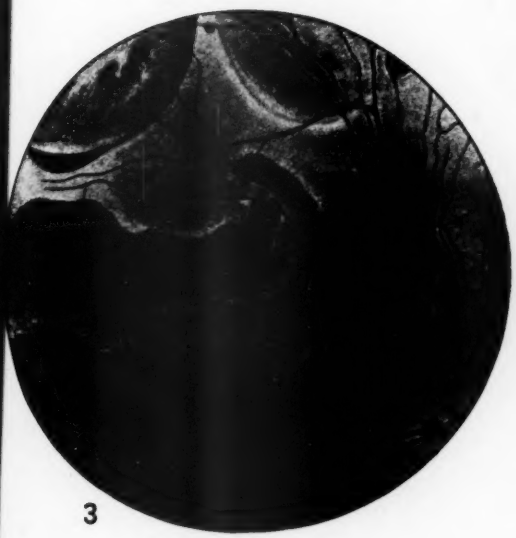

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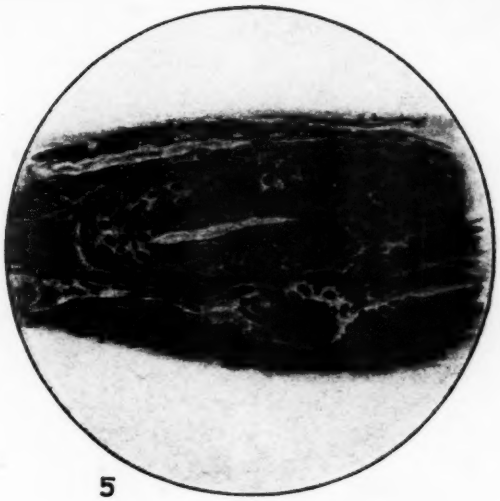

5

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pigmented and nonpigmented retinal scars, opacities of the vitreous, including synchisis scintillans, and cataract.

While it has not yet been encountered in monkeys, perivasculitis similar to that seen in the eyes of hypertensive persons has been frequently noticed in the eyes of hypertensive dogs (figs. 1 to 5). An irregular white patch appeared on a retinal artery or arteriole, usually between the origin of the blood vessel at the nerve head and the visible periphery of the retina. Once established, the white area never disappeared, but new areas appeared, coalesced and gradually spread along the artery and its branches. In the earlier stages of sheath formation, the affected blood vessel could be seen through the white covering as a narrow pink streak. Later, when the arterial covering was more dense, the vessel disappeared and was represented by an irregular white streak slightly wider than the original blood vessel. Ophthalmoscopically, the portions of the blood vessel visible through the white covering had a pink color and apparently carried blood. When an artery was completely covered, it was not possible to evaluate its functional condition. The ophthalmoscopic picture presented by perivasculitis was quite distinct from that of the silver wire artery or arteriole. The outline of the silver wire vessel was cleancut, and the vessel was smaller than it was originally. An arteriole with perivasculitis presented a slightly irregular outline, had a soft moth-eaten appearance and was wider than it was originally.

No monkeys have been observed with malignant hypertension. The eyes of the dogs with acute or malignant hypertension presented a picture of rapid and extensive visual damage. In dog 3-8, coincident with damaged renal excretory function, complete detachment of the retina, massive intraocular hemorrhages and secondary glaucoma with ulceration of the cornea occurred. This dog already had evidence of extensive retinal vascular disease and had been hypertensive for about three years (fig. 1).

An outstanding example of the malignant phase of hypertension occurring in an animal with previous hypertension was observed in dog 2-50. The right main renal artery was constricted, and the blood pressure rose to a maximum direct [3a] pressure of 240 mm. of mercury. The right kidney was then removed. The blood pressure promptly returned to normal and remained normal. The main renal artery of the remaining kidney was greatly constricted. The mean blood pressure rose again and in the course of about one month exceeded 300 mm. of mercury. Evidence of disturbed renal excretory power appeared. The animal became uremic. The urea nitrogen content of the blood was 83 mg. per

3a. By direct or mean blood pressure is meant the pressure determined by inserting a needle connected with a mercury manometer directly into the femoral artery.

hundred cubic centimeters just before death. Blood appeared at the anus, and within a short period before death both eyes became filled with blood. Previous to the malignant phase of the hypertension, the only visible change ophthalmoscopically was doubtful tortuosity of the nasal retinal arteries (fig. 6).

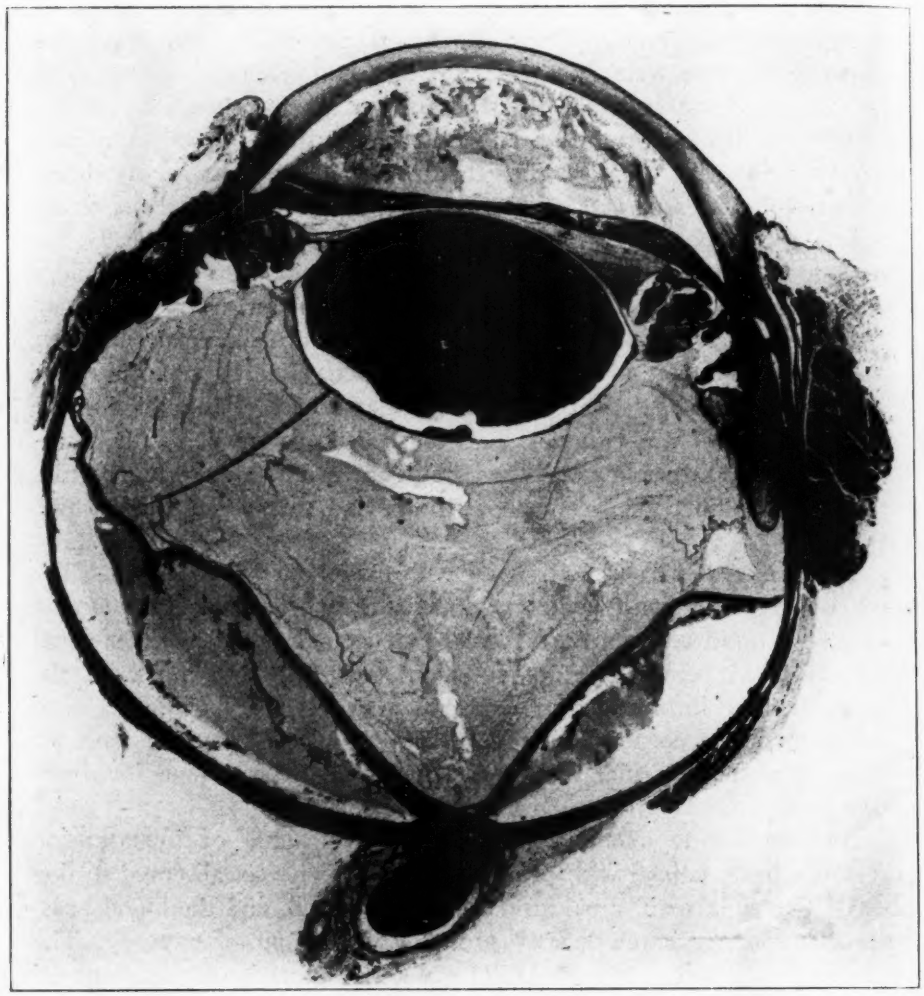

Fig. 6 (dog 2-50 L. 45).—A section of the left eye of a dog with malignant hypertension following prolonged benign hypertension. The eye contained bloody fluid rich in fibrin. The retina was detached. There was marked edema of the ciliary processes.

An example of the acute malignant phase of hypertension produced purposely by the same sequence of procedures employed in dog 2-50 was observed in dog 3-39. The details of the experimental history of

this animal will be given here because they were omitted accidentally from a previous publication,[18] in which this should have appeared.

The dog was a young virgin, black and white mongrel collie, weighing 10 Kg. on April 20, 1937, when the determination of the normal pressure was begun. On July 8 the left main renal artery was clamped slightly. The mean blood pressure became elevated, reaching a maximum of 165 mm. of mercury. This persisted until July 30, at which time the blood pressure was 160 mm. of mercury. On this day the left kidney was removed. The blood pressure on the next day was 150 mm. of mercury. With minor variations the blood pressure persisted at the normal level for this dog until September 22, on which day the right main renal artery was greatly constricted. The blood pressure became promptly elevated and rose gradually to 255 mm. of mercury, the maximum pressure which was reached on October 25. On this day the blood urea nitrogen was 18 mg. and the creatinine 1.5 mg. per hundred cubic centimeters. The next day the urea nitrogen increased to 32 mg. and on October 29 it was 150 mg. At this time the animal appeared extremely ill. It died on October 31.

On October 26 the eyes, which previous to the final operation were normal, showed a rapidly increasing edema of the papilla and retina. The tapetum lost its bronze appearance. It appeared gray, owing to diffuse edema. In addition, it was observed that the pupils were unequal, irregular and small. In the right eye small round retinal hemorrhages were scattered along the nasal vessels. On the temporal side of the optic nerve and high up in the retina were small sheets of hemorrhage. The left eye had a few small scattered hemorrhages along blood vessels. Four days later both pupils were widely dilated and inactive to light. In the left eye there were streaks of pale brown bloody fluid on the anterior lens capsule and in the anterior chamber. The details of the fundus were indistinct. The fundus of the right eye was faintly seen. A few new hemorrhages were present. The vitreous was hazy, and the retina was edematous and detached. Tension to touch was normal to minus (fig. 7).

The acute malignant phase of hypertension has been produced in several dogs without a previous period of the benign phase by marked constriction of both renal arteries at the same time or with an interval between constrictions and also by great constriction of the aorta just above the origin of both renal arteries. The eyes of these animals have not yet been examined histologically, but the vessels of the rest of the body showed the same changes as in dogs 2-50 and 3-39.

The histologic examination of the eyes of dogs with malignant acute hypertension revealed severe degenerative disease of the arterioles of the uvea, together with extravasations of blood into the uvea and retina, papilledema, edema and detachment of the retina and subretinal and intraocular serofibrinous exudate.

The walls of some arterioles in the retina showed marked edema (fig. 8). The arteries and arterioles of the choroid, ciliary body and iris, however, exhibited widespread degenerative changes. There was evidence of collagenous and hyaline degeneration of the wall of the vessel (fig. 9), as well as necrosis of the wall, intramural edema and hemorrhage, perivascular hemorrhage and localized areas of lymphocytic perivascular infiltration (figs. 5 and 10).

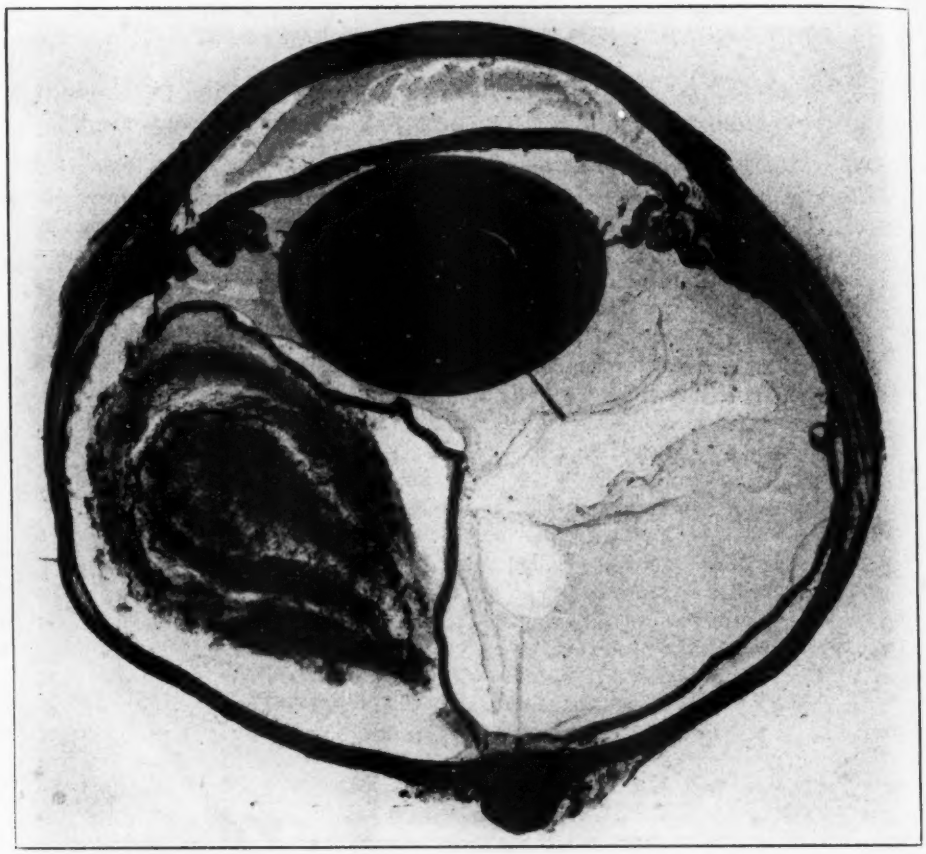

Fig. 7 (dog 3-39 L. 86).—A section of the left eye of a dog with acute malignant hypertension. There are swelling of the papilla and edema and detachment of the retina and choroid. The eye was filled by a bloody serofibrinous fluid.

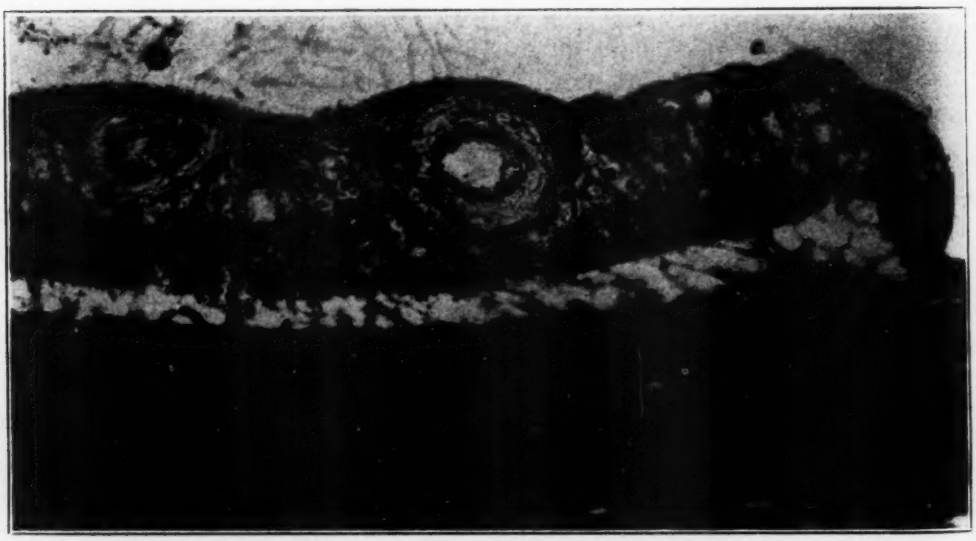

Fig. 8 (dog 3-39 R. 40).—Two edematous retinal arterioles at the ora serrata; × 200.

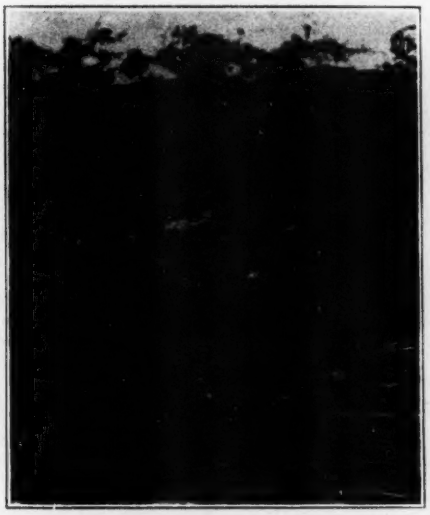

Fig. 9 (dog 3-39 L. 40).—Choroidal arteriole with swollen, partly hyalinized wall and collagenous degeneration; × 200.

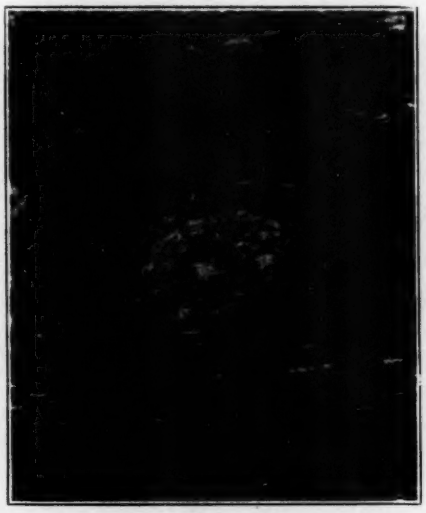

Fig. 10 (dog 3-39 R. 45).—Choroidal blood vessels showing edema and fibrinoid degeneration of the wall of the vessel, mainly subintimal; × 200.

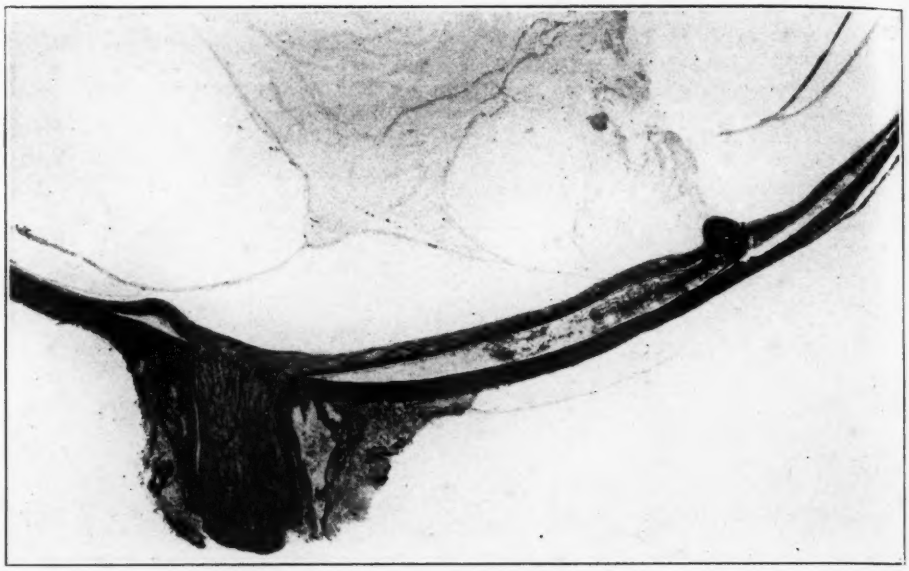

Fig. 11 (dog 5-9 R. 45-A).—A low magnification of a section of the back of the eye. The retina is detached and undergoing degeneration. A nodule of unusual appearance is located in the retina.

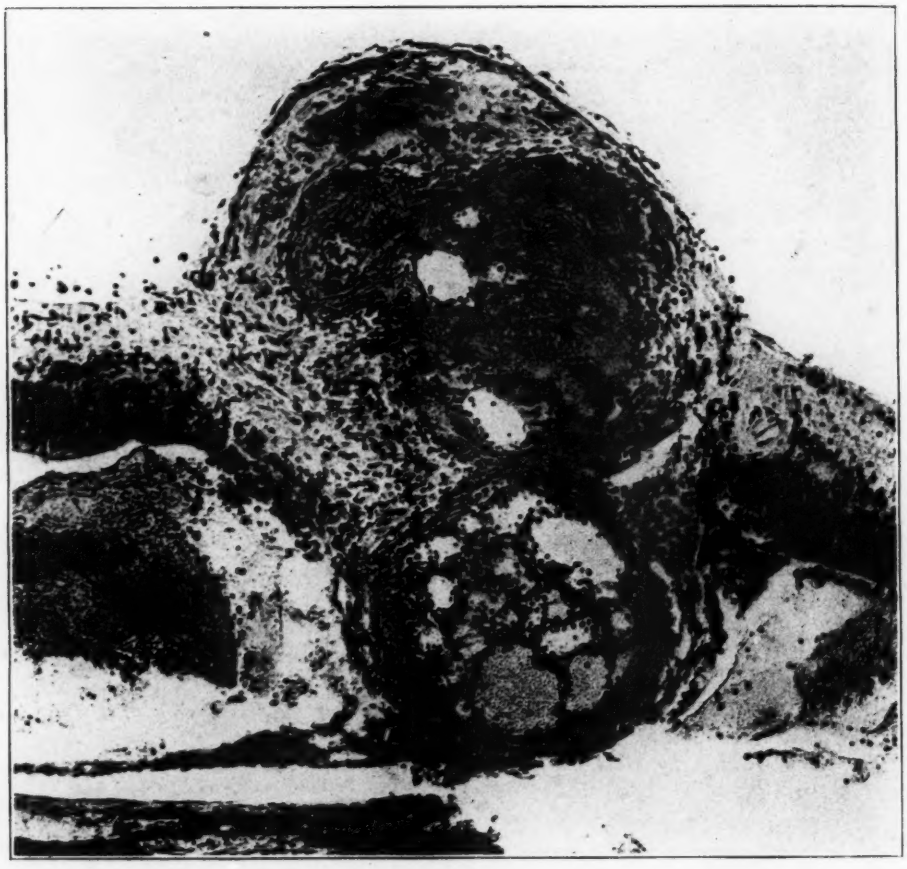

Fig. 12 (dog 5-9 R. 45-B).—A higher magnification of the nodule shown in the retina in figure 11; × 116. The upper portion of the nodule shows an area of hyalin containing vascular spaces. In the lower portion of the nodule is a thin-walled blood vessel, the lumen of which is divided by many partitions.

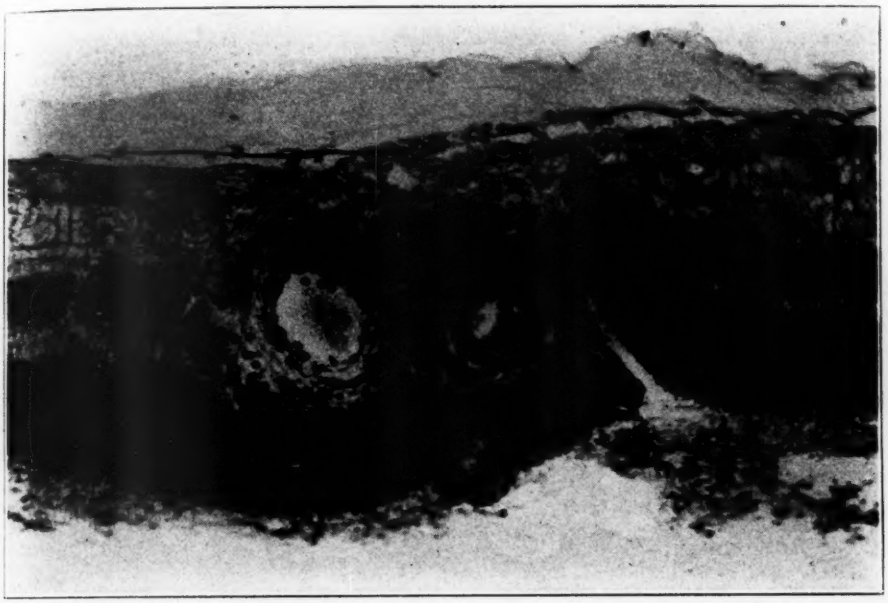

Fig. 13 (dog 5-9 R. 105).—An arteriole and a vein in a portion of degenerated detached retina; × 179. The wall of the arteriole is unusually thick. The quantity of perivascular tissue is also abnormally great.

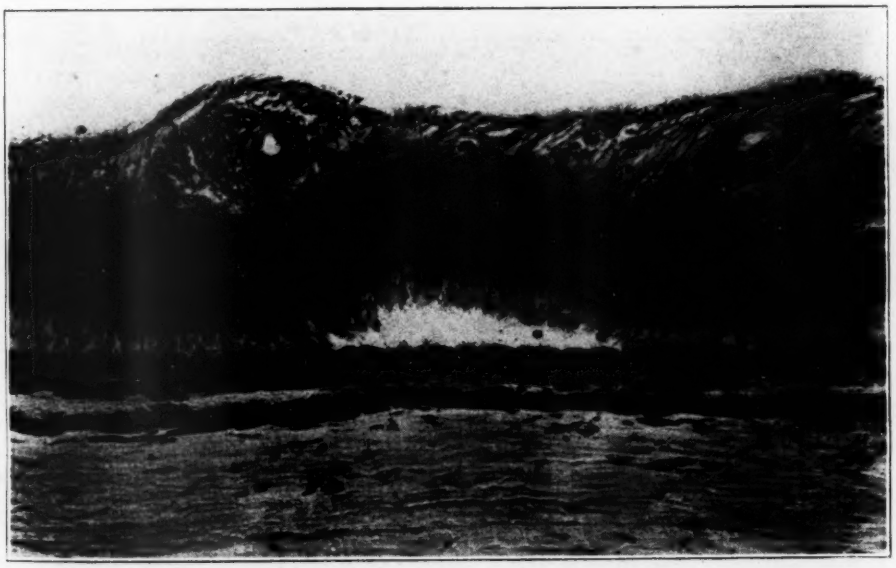

Fig. 14 (dog 6 R. 18).—An arteriole in a slightly edematous retina. Surrounding this diseased arteriole is a large quantity of slightly edematous adventitia. Hematoxylin and eosin stain; × 173.

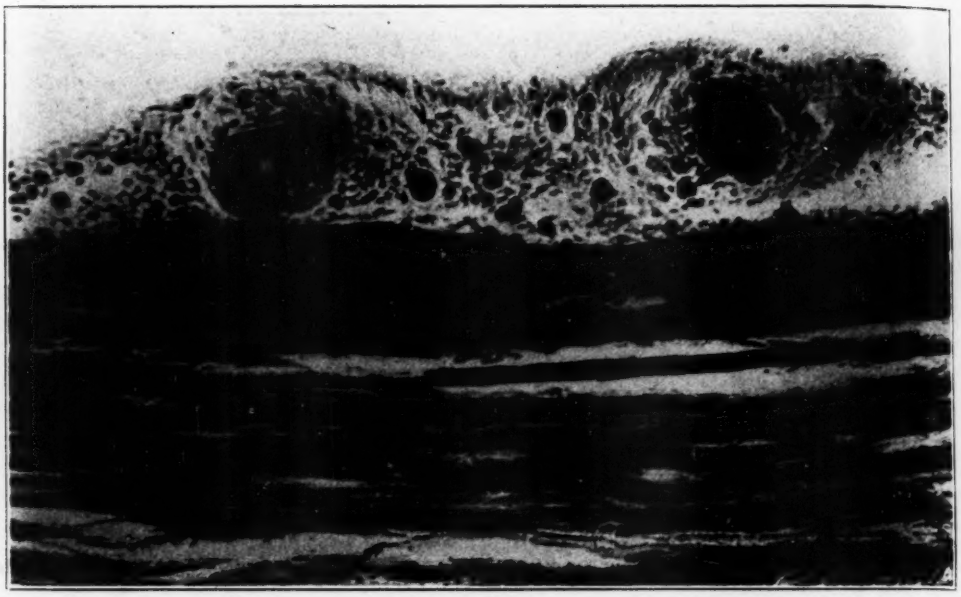

Fig. 15 (dog 6 R. 17).—A portion of degenerated retina containing two diseased arterioles. Marked proliferation of elastic tissue and perivascular tissue are shown. Weigert's elastic method; × 173.

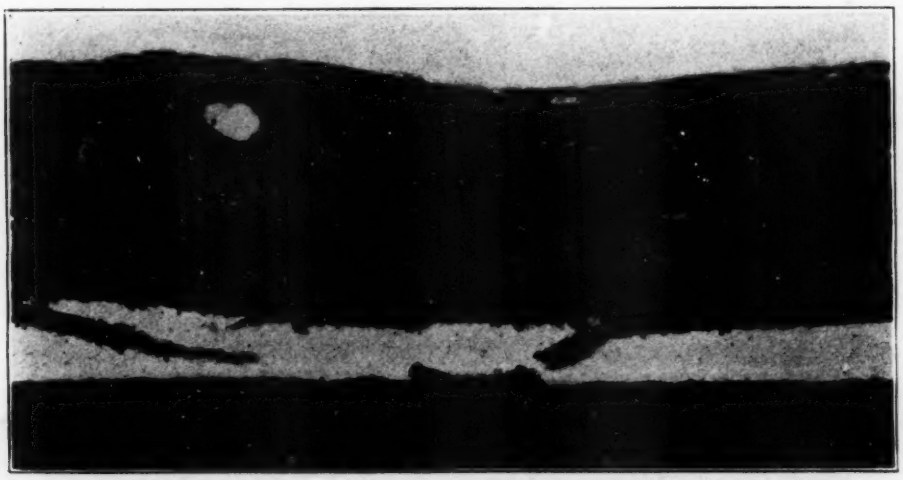

Fig. 16 (monkey 5 L. 81).—A retinal arteriole showing multiplication of elastic tissue and a thick adventitia. There is marked multiplication of capillaries in this region. Weigert's elastic tissue stain.

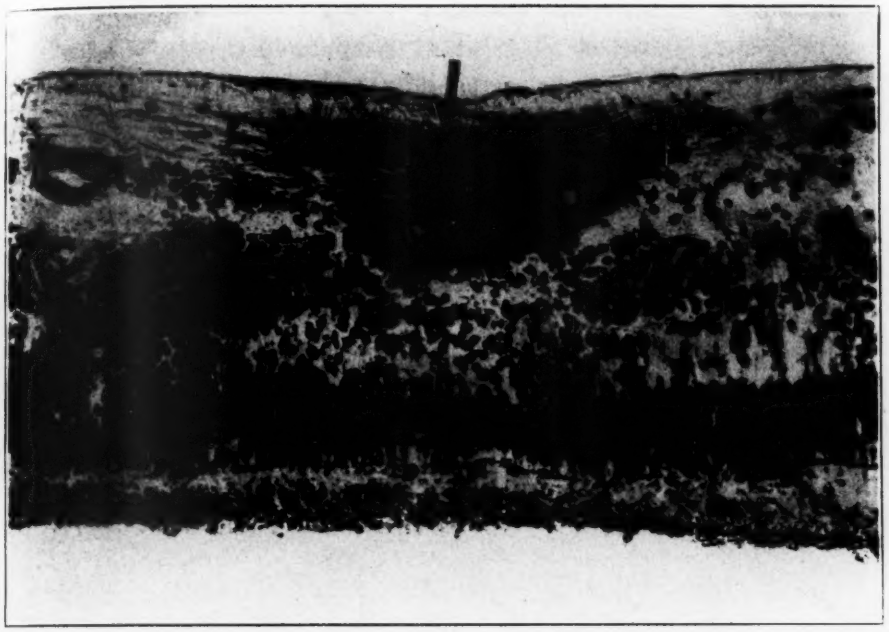

Fig. 17 (monkey 5 L. 156).—Dense red staining area in retina, probably hemorrhagic remains (indicated by arrow). Hematoxylin and eosin stain; × 215.

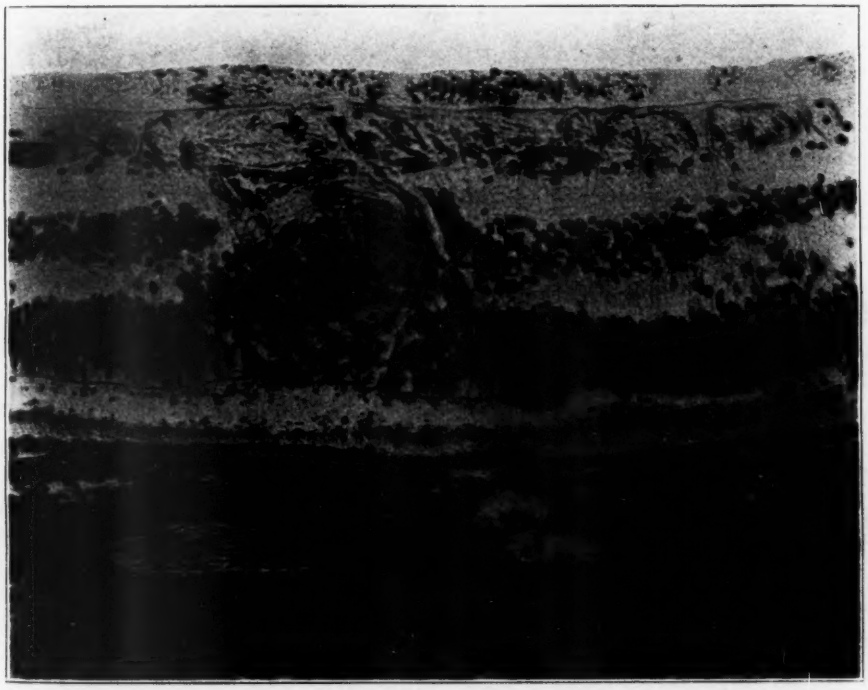

Fig. 18 (monkey 5 R. 45).—Marked adventitial proliferation around two small closed blood vessels in the retina; × 186.

In animals that had a period of benign hypertension before the malignant phase acute degenerative necrotizing lesions were superimposed on chronic arteriolar disease. Arterioles with similar degenerative and necrotic changes were present elsewhere in the bodies of these animals.[18]

In dogs with persistent hypertension with moderate or no disturbance of renal excretory function (the group with benign hypertension) no instance of macroscopic or microscopic papilledema has occurred. Localized areas of retinal hemorrhage and edema were present, but only in hypertensive animals with terminal renal damage was widespread

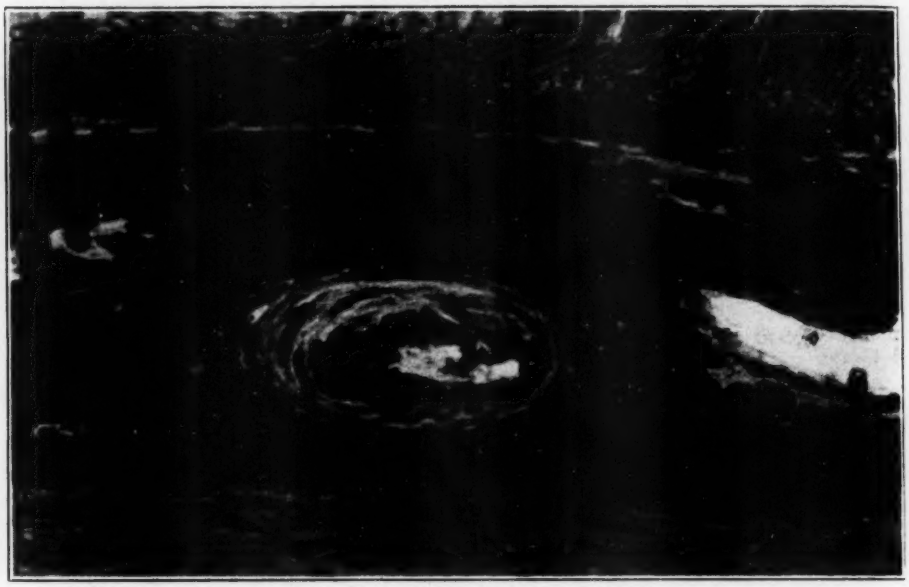

Fig. 19 (monkey 5 R. 25).—Choroidal arteriole showing a thick wall and hyaline degeneration of the intima. Weigert's elastic tissue stain showed that the elastica of this vessel was destroyed. Hematoxylin and eosin stain; × 130.

edema of the retina or choroid present. Retinal scars, in some of which there was iron-containing pigment, were present in the eyes of several animals (figs. 11 and 12). Partial atrophy of the choroid was noted. Diseased retinal arteries with thick walls were seen. The thickening of the wall was most frequently caused by a thick media, although in some animals the intima showed definite evidence of thickening and degeneration, particularly hyalinization. The blood vessels in the portion of the retina where perivasculitis had been seen ophthalmoscopically frequently showed a thickening of the adventitia and perivascular cellular elements (figs. 13 and 14). Some retinal arterioles showed evidence of disease of all three coats. With special stains for elastic tissue, large

quantities of elastic fibers were shown to be present in many of the small arteries or arterioles (fig. 15). The choroidal arteries and arterioles of benign hypertensive dogs, beyond a rather general thickening of the wall of the vessel because of a thick media, did not show evidence of involvement of the adventitia or, except in a few instances, disease of the intima. The posterior and anterior ciliary arteries and the arterial vessels of the ciliary body and iris did not show much evidence of disease; neither was there much, if any, increase in the number of their elastic fibers.

A monkey with benign hypertension had ophthalmoscopic evidence of severe disease of the retinal vascular tree. The retinal arteries were small, and many resembled copper wires or silver threads.

Histologically, the retinal arteries showed a moderate degree of disease mostly confined to the media (fig. 16). The choroidal arteries, on the contrary, had widespread and advanced disease of the intima and media (fig. 19). The arteriolar disease in this monkey was similar to that found by Moritz and Oldt [4] in hypertensive persons with arteriolar sclerosis.

COMMENT

Papilledema did not occur in dogs with the benign type of experimental hypertension as long as the excretory function of the kidney remained normal. Decreased renal excretory power usually ushered in ocular changes characterized by edema and detachment of the retina, papilledema and hemorrhages.

The ophthalmoscopic picture was a guide to the nature and extent of the vascular changes in the eyes and bodies of dogs with acute malignant hypertension. Changes seen ophthalmoscopically in dogs and monkeys with benign hypertension were of only relative diagnostic and prognostic value. The degree of apparent involvement of the retinal arteries was not always confirmed histologically. The type and extent of disease in the arterioles of the eye frequently differed from that found in the body. It was impossible during life to evaluate the condition of the uveal blood vessels. The distribution of ocular and systemic arteriolar disease was segmental and comparable to arteriolar sclerosis in man.

SUMMARY

The eyes of dogs and monkeys with persistent hypertension following constriction of the main renal arteries have been observed for more than five years. Changes similar to those seen in man with benign and malignant essential hypertension occurred in the eyes of these animals.

4. Moritz, A. R., and Oldt, M. R.: Arteriolar Sclerosis in Hypertensive and Non-Hypertensive Individuals, Am. J. Path. **13**:679, 1937.

ABSTRACT OF DISCUSSION

DR. ARTHUR J. BEDELL, Albany, N. Y.: It seems proved that sex, heredity, environment and infections all play a part in the terminal composite picture of hypertension in human beings. These factors cannot be appraised in animals. Then, too, there is the relationship of the control mechanism of the sympathetic nervous system which cannot be considered similar in animals and in human beings. This suggests the question of operative intervention for the hypertension, but it is outside of the scope of either the thesis or this discussion.

The authors' group of animals with benign hypertension, without a renal lesion, is the largest. There seems to be no hard and fast rule which determines whether in a given case hypertension will be of the first type, with early retinal hemorrhage and edema and early moderate and later severe retinal vascular disease, or of the second type, with slowly progressive vascular changes, hemorrhages and small areas of edema.

Patients with benign hypertension are observed for decades with little or no change in their condition from year to year, and then suddenly, often without any discoverable cause, these patients become worse and die. Furthermore, death may supervene when the retinal exudates and hemorrhages have almost disappeared, when they are increasing or when they seem to be stationary. Therefore, until the general condition of the patient is known, it is impossible to determine far in advance when any benign hypertension will end. As yet animal experiments have not solved this riddle.

A number of women with a high diastolic pressure and a systolic pressure of 250 mm. of mercury did not show the same fundus picture. This is understood by those who know the infinite variety of fundus patterns, and yet it offers an insurmountable hazard against an ex cathedra prognosis. An acute toxic fundus in a patient with evidence of general distress exhibits alarming signs such as papilledema, extensive and increasing exudates with hemorrhages. These changes are comparable to those found by the authors in their animals with malignant hypertension. The practical point is that high blood pressure should not be considered the only essential in prognosis.

Persons with malignant hypertension are a detached group. Unmistakable signs are seen in some, while in others they are less evident, and the disease is diagnosed correctly only after an observation period of variable time, although those with frank, serious involvement may on their first visit show edema of the retina with fulness of the vessels. This type of hypertension is sometimes difficult to diagnose and usually discouraging to treat. Even if the patient has high blood pressure and a severe intolerable headache, the changes in the fundus may be few. These symptoms in the presence of a typical papilledema have led to intracranial explorations for suspected tumor of the brain, and sometimes the pressure has overshadowed a definite cerebral neoplasm. The retinal edema may be general, and exudates and hemorrhages may be absent or present.

The malignant hypertension observed by the authors in dogs resembles more nearly the human form, but differs in three ways. First, the authors, at least in the abstract which they read, did not refer to the massive exudates which are a conspicuous part of the fundi of many persons with long-standing hypertension. These exudates may be about

the macula, the so-called circinate retinitis; they may be large, flat, thick, less definitely outlined areas at the posterior pole, which frequently produce glistening iridescent plaques; linear exudates like spokes from the hub of a wheel, or isolated collections without regular outline. Secondly, the authors say nothing regarding gross vascular accidents, such as embolism, endarteritis, thrombosis or phlebitis, which are not unusual expressions of hypertension. Thirdly, the terminal stage, in which they found the animals' eyes filled with bloody fluid, does not seem to be duplicated in man. The nearest approach to it is in the cases of enormous retinal and vitreous hemorrhages caused by excessively high pressure complicated with diabetes, thrombosis or embolism. Perhaps the duration of the process accounts for these differences. Manifestations of hypertension develop rather rapidly in the laboratory within a few months. This gives little time for the establishment of collateral circulation and the formation of certain exudates.

The authors constricted the renal arteries and noted subsequent changes in the fundus. This is not analogous to any human illness, and their deductions considered from that restricted field are suggestive but not conclusive. The changes were too rapid, not similar to the slow induction of most hypertension, and are frequently more like the acute changes in some toxemias.

They have advanced one more proof of the effect of high blood pressure on the ocular fundus. Their work was carried on in a most scientific manner, their conclusions were justified by their observations, and they merit commendation and deserve praise.

Dr. William L. Benedict, Rochester, Minn.: It has been definitely established that elevation of systolic and diastolic arterial pressure is associated with the renal ischemia resulting from constriction of the main renal arteries in experimental animals. However, the mechanism of this elevation of blood pressure has not been proved as yet. Probably the most logical theory is that a vasopressor substance of hormonal type, produced or no longer inhibited in the ischemic kidney, initiates and maintains in the peripheral arterioles throughout the body a functional constriction which may be followed later by organic changes in the walls of the vessels. If this is true, it might be assumed that constriction of the retinal arterioles would occur as a part of the generalized vasoconstriction. Page stated that this narrowing of the retinal arterioles does occur in dogs. Apparently, however, the authors have noted this initial constriction only in monkeys. It might be possible to determine whether or not this actually occurs by measurements of the retinal arterioles before and shortly after the development of the hypertension. Apparently, the blood pressure rises rapidly after the production of bilateral renal ischemia and reaches its maximum within a few days. Subsequently it remains at this level or, in a few cases, it may drop somewhat, perhaps owing to the establishment of collateral circulation to the kidneys. If the induced hypertension were directly comparable to acute primary hypertension in man, one might expect the early development of retinitis. This has recently been found to be the case by Dr. Keyes and Dr. Goldblatt in dogs in which there developed extreme hypertension after removal of one kidney and marked restriction of the renal artery in the remaining kidney.

As in all previous experiments whereby hypertension and nephritis are produced in animals, the retinal lesions observed are not identical

with those seen in man. That this may be due to a species rather than to a disease difference is suggested by the difference in the ophthalmoscopic pictures observed by the authors in dogs and in monkeys. In particular, from the histologic standpoint, the cytoid bodies and the serofibrinous exudates in the internuclear layer of the retina have not been described.

In general, one forms the impression that the changes which the authors have found in the dogs' eyes and which they characterize as late manifestations of the syndrome are of the inflammatory type. The heavy and progressive periarterial sheathing has no exact counterpart in the hypertensive retinal picture in man; and the hemorrhages into the vitreous and the accompanying scarring and proliferative changes in the retina are not seen in human beings with hypertension uncomplicated by infection or venous thrombotic disease.

It would seem certainly that the lesions observed by the authors are not associated with retained nitrogenous waste products. And further, no toxic product of disturbed renal metabolism has been demonstrated in the blood of these animals. In monkeys, in which the retinal lesions more clearly simulated those seen in man, visible lesions in the arterioles of the retina apparently preceded the development of retinitis. The retinitis healed, while the vascular lesions appeared to progress, as is the case at times in human beings with hypertensive disease. These facts, along with the histologic changes of less marked organic vascular disease than would be expected from the retinal picture, suggest at least that a part of the ophthalmoscopically observed changes in the arterioles were of functional or angiospastic type and that the preliminary functional changes which are generally accepted as the precursors of organic vascular disease in the rest of the body may have been responsible for the transitory retinitis. If so interpreted, the retinal lesions in this case might well be compared to the sequence of events in the hypertensive toxemia of pregnancy.

On histologic examination of the eyes of these experimental animals, the authors found changes of varying type and degree in the media and intima of the retinal and choroidal arteries and arterioles. Similar variations are to be seen in the retinal vessels of human beings with hypertensive disease.

It seems justifiable to conclude from Dr. Keyes and Dr. Goldblatt's observations, at the very least, irrespective of questions regarding the pathogenesis of the retinitis, that the retinal and choroidal arteries and arterioles are involved in a similar manner and in a comparable degree with those of the rest of the body in a generalized arteriolar disease induced by prolonged vasoconstriction in experimental animals as they have seemed to be in man.

Dr. John E. L. Keyes, Cleveland: The retinal arteries of the dog are smaller than the retinal arteries of man. Ophthalmoscopically, it is difficult to see spasm of the retinal arteries of the dog. The ocular fundi and the retinal blood vessels of the monkey (macaque) closely resemble those of man. Spasm of the retinal arteries is more readily recognized in monkeys than in dogs.

I have seen perivascular sheaths in the eyes of persons with essential hypertension. The changes noted clinically and histologically in these experimental animals compare very closely with changes seen in the eyes of persons with benign and acute essential hypertension.

READING DIFFICULTIES IN CHILDREN

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Educators are today making every possible effort to teach children to read well. Formerly children who failed to learn to read lived out their school lives in classes between the third and the fifth grade and were dismissed to the industrial world at the age of 14. Now every child is required to remain in school in Pennsylvania until he is 18, and he must be placed in classes beyond these low grades in order to complete his social development. The use of general testing for the intelligence quotient of each child weeds out and places in special classes those who cannot learn. There remains, however, a group of children with intelligence quotients of normal or better than normal and with a normal social and vocabulary development who fail to learn to read as well as the average of their class. The ophthalmologist is being asked with increasing frequency to examine these children to see if any visual difficulty is associated with the failure to learn to read.

Another factor of modern educational procedure sends more children than formerly to the ophthalmologist's office. Methods of teaching reading have changed. The newer method, as shall be shown, requires a greater span of visual attention but results in ability to read rapidly. Beyond the third grade the amount of supplementary reading required is based on this ability to read rapidly, and the child who reads slowly, even though accurately, tends to fall behind his grade. Symptoms of eyestrain are a frequent concomitant of the effort of such children to keep up with the required reading, and they also are brought to the ophthalmologist for consultation.

A review of the methods of teaching reading is necessary if the ophthalmologist who studied in the first grade from twenty to forty years ago is to understand the problems of the present day child. Some will remember being taught the letters of the alphabet by their sounds and then being taught how to combine the individual letters into words. Later it became evident that a child learned to read more quickly if he read whole words already in his vocabulary. After learning these words, he learned the family of words and derived the essential phonic sounds which he might use in analyzing new vocabulary. Still later, the word

method was expanded into a phrase method, but in most classes of today it has been further expanded into a sentence method. The child immediately on entering school learns to read whole sentences which express facts and actions familiar to his experience. The analysis of the sentence into individual words and the analysis of the individual word into phonic sounds are taught as a secondary matter when the child is already reading an extensive vocabulary based on visual memory rather than on synthesis of sounds.

It has long been a custom to consider a child ready to learn to read when he is 6 years old. Today many educators are making studies of so-called "reading readiness" and are inclined to believe that certain children are not prepared to read although they have reached their sixth birthday. This conclusion may be fallacious in that it is based on the fact that certain children with apparently normal equipment fail to learn to read at this age. The final conclusion on the subject of "reading readiness" must await more research; in the meantime, the vast majority of the children will be required to try to learn to read when they are 6.

It is at once apparent that a child with gross visual defects will probably fail to learn to read. However, in many schools there is no ocular examination for visual acuity until the third grade or beyond, so the child who fails in reading because of gross visual errors is not detected unless his parents take him to an ophthalmologist. Ophthalmologists who contact public school systems should urge immediate examination for all children entering school by means of illiterate charts to detect and correct major visual errors. At the end of the first year all children who are unable to read should be given a thorough examination, including refraction under atropine.

In this paper we shall not discuss further the question of visual acuity but will concern ourselves with the less obvious problems of the children who cannot read. The modern sentence method of teaching reading, while it produces rapid and intelligent readers, tests to the limit the child's powers of attention and concentration. Many of the problems of the child who is unable to read are matters more for the teacher and the psychologist than for the physician; but the doctor is directly interested in the various factors affecting visual attention. Because of the high degree of visual attention required, certain minor defects that were of less importance under older methods of teaching have now become significant.

VISUAL IMMATURITY

The first of these factors is immaturity of the child's visual apparatus. This is expressed in one way by poor resolution. If all children entering the first grade were tested for visual acuity, it would be found that the majority of them do not have full 6/6 vision. A second test

at the end of the year, or at the beginning of the second year, would show that most of them have normal vision. This is simply due to the fact that the child's resolving power has not yet been fully developed because of lack of visual experience. He may have a perfectly sharp retinal image but has never been called on to resolve and interpret that image into a symbol with meaning. The condition is of no importance and may be regarded as normal. All teaching, however, should be done by means of large charts and blackboard demonstration rather than by the use of printed books, so that the power of resolution may develop before it is necessary for the child to resolve small print.

A second evidence of immaturity is expressed in the reversal phenomenon. This may be apparent as reversal of words, letters or entire sentences. The reversal of letters is common to almost all children of from 4 to 6 years, and any one who tests visual acuity of children has noticed that they frequently reverse the position of two letters or numbers in the test line. Reversal of short words, such as reading "saw" for "was," is fairly common during the first few months of reading. A variation of the same condition is the perception of the end syllable for the first part of the word. In reading the word "running" the child may pick up the last syllable, substitute a word already in his vocabulary, and read "walking." The highest degree of reversal is reached in mirror writers, who reverse entire sentences and write them backward.

The cause of reversal may be simple immaturity or some confusion in the eye association pathways. This confusion may be due to poor interpretation of images as a result of confusion in eye-hand association. This last condition may be found in a left-handed child who is being taught to use his right hand or in a right-handed child from a family with a strain of left-handedness or in an ambidextrous child. A child sensitive to low hypermetropia will frequently show reversals.

The treatment of reversal is more a problem for the teacher and the psychologist than for the ophthalmologist, but the oculist should recognize the condition and oversee the training, as the child may be caused considerable difficulty if he is not handled properly. Reversal due to simple immaturity will disappear spontaneously as the child develops, and the only treatment necessary is the planning of the reading program in such a way that the child is given as few reversible words as possible. The child with a crossed eye-hand dominance requires more careful attention. This is particularly true of the right-handed child with a family history of left-handedness, as the hereditary situation may be overlooked. Treatment consists in determining which is the dominant eye and in having the child use the hand on the same side. Proper eye-hand coordination can be developed by tracing, drawing or mechan-

ical activities. An excellent exercise consists of tracing in a stereoscope, as in the training of amblyopia, with the pencil in the hand corresponding to the dominant eye. In the case of mirror writing it must be impressed on parents and teacher that the condition should not be drawn to the child's attention. If the child becomes aware that he is an object of interest, he will continue mirror writing deliberately and indefinitely. When a sentence is written backward, the child should trace the corrected sentence and then write it properly free-hand.

The entire treatment of reversal is concerned with the clearing of the eye-hand association pathways to avoid confusion. Occasionally a situation arises in which it is necessary because of the demand on the part of the parents, the teacher or the child himself to train a left-handed child to use the right hand. If the left eye is strongly dominant, this will result in poor muscular coordination, poor reading and possibly speech defects. The best way to handle such a situation is to occlude the left eye and train the right hand and the right eye to work together in an attempt to change the ocular dominance to the right eye. Parsons stated that once ocular dominance is established, it cannot be changed by training. The age at which it is acquired is not exactly known, but it probably begins at about 3 years and is firmly fixed at the age of puberty. Even if ocular dominance is not changed, the right eye-right hand coordination in left-handed children can be improved with consequent improvement in reading and writing.

By no means all left-handed children show reading or speech difficulties if they are taught to use the right hand, but many of them do have these difficulties, and the possibility must always be kept in mind in the case of such children. An excellent review of the subject of ocular dominance has recently been published by Fink.[1]

LOW HYPERMETROPIA

Another cause of poor reading ability in children in the first grade is low hypermetropia. This is somewhat difficult to explain, but probably is another evidence of immaturity. A child of 6 has an accommodative power of 15 diopters, and simple hypermetropia up to 1 diopter may be regarded as normal at this age. With this power of accommodation, it does not seem possible that simple hypermetropia between 1 and 2 diopters could cause any difficulty, but the clinical fact remains that we have seen many children progress from near the bottom of their class in reading to near the top simply by the correction of hypermetropia of between 1 and 2 diopters. Since this seemed so illogical, we checked carefully with the teachers and parents to make sure there had been no

1. Fink, W. A.: The Dominant Eye: Its Clinical Significance, Arch. Ophth **19**:555 (April) 1938.

change in teaching methods or special tutoring. We do not believe that the improvement in reading was due to the psychologic effect of wearing glasses, as several of the children objected strenuously to them.

The great majority of children show no signs or symptoms from low simple hypermetropia, and our only explanation of the fact that a few of them do is based on the theory that these children have not learned to use their accommodation in a perfectly automatic, subconscious manner. Apparently some few children with low refractive errors find it necessary to pay a certain amount of attention to the mechanics of accommodation, which in other children more visually mature is perfectly automatic. This calling of attention to the act of accommodation and the necessity for concentration on the retinal image in order to keep it clear distract the child's attention from the sentence which he is supposed to be reading. We have already stated that the sentence method of teaching requires all the visual attention of which a 6 year old child is capable. By this distracting of attention the act of accommodation probably is responsible for inability to learn to read by the sentence method. We find that by the time the child has reached the third or fourth grade, after correction in early reading, he is able to read with ease and comfort without glasses even though the hypermetropia remains unchanged. This leads us to believe that in this particular type of child we are dealing with another type of visual immaturity. The child has a superabundance of accommodative power, but because of lack of practice has not learned to use it with perfect ease and lack of conscious effort. As he progresses in age and visual experience, the function of accommodation becomes automatic and requires no attention on his part. This is one of the conditions which has become important because of modern methods of teaching reading. Under the word or phonic systems, low hyperopic errors were of no significance because the child could pay attention to the act of accommodation and still have sufficient span of visual attention to read single letters or words. Many such children never learned to read rapidly, although "sentence reading" was introduced in the upper grades. The methods now used in the first grade produce more excellent readers and fewer "word" readers; but it is evident that more children will need visual aids.

DEFICIENT FUSION

All the foregoing factors in deficient reading ability may be regarded as various types of visual immaturity. Another cause of poor reading is deficient binocular fusion. In the examination of several hundred children in the first grade we found no significant fusion difficulties except in those children who had a squint, those who had had a squint and those whose vision was markedly better in one eye than in the

other. The children with squint or with squint which is partly corrected may be divided into four groups: those with uncorrected monocular squint, those with partly corrected monocular squint, those with uncorrected alternating squint and those with partly corrected alternating squint. The phrase "partly corrected" may be interpreted to indicate any stage in the recovery of the squint after refraction, operation or orthoptic training in which full binocular vision with complete ranges of fusion has not yet been established.

Uncorrected monocular squint will cause no reading difficulties, as the child's suppression is complete and there is no binocular confusion. Orthoptic training may be continued during the school term. Occlusion for amblyopia is best done outside the school, and the most satisfactory training consists of drawing and tracing rather than reading of print so that confusion in reading as amblyopia improves may be avoided as far as possible.

Partly corrected monocular squint is a frequent source of reading difficulty. This situation may be expected in a child whose squint has been cosmetically cured by refraction or by operation without adequate training in fusion. The remaining suppression or alternation produces binocular confusion, which makes it impossible for the child to read by the sentence method. It must be remembered that during the course of orthoptic training monocular squint passes through a period of alternating squint, which is confusing to a child if he is learning to read during this period of his training.

In such a situation the best course is to have the child occlude one eye while he is in school to avoid the binocular confusion which results from the rapid alternation. Occlusion is applied to the right and the left eye on alternate days. Orthoptic training should be pushed as rapidly as possible.

There is another factor in cases of cosmetically corrected squint which causes reading difficulty and which is frequently overlooked. This is poor fusional convergence. It seems paradoxic that a child who has had convergent strabismus is unable to converge, but the situation is explained by the fact that a child with squint does not use true binocular or fusional convergence. This will develop spontaneously in many cases after correction of the squint by refraction, orthoptics or operations. But in many more cases the fusional convergence remains weak and causes excessive tiring of the eyes or confusion, perhaps even alternation developing at the near point. This should be kept in mind in the treatment of all children with convergent squint, and the training should be directed not only at the turning of the eyes but at the development of proper fusional convergence.

The treatment is, of course, orthoptic training. During the school year the child can be made much more comfortable either by occluding

one eye to avoid the necessity for binocular vision at the near point or by the use of base-in prisms to give binocular vision at the reading distance without the necessity for convergence. Usually orthoptic training over one summer's vacation will develop fusional convergence to nearly normal.

In cases of alternating squint we believe that it is best not to start training until the child has learned to read. The period of training is long and tedious and always produces visual confusion, which makes it difficult for the child to learn to read during the training period. A careful history should be taken in all cases of apparently alternating squint to make sure that the condition is not an original monocular squint which is in the stage of alternating in the process of spontaneous recovery.

If this is true, or if it seems advisable to correct the squint while the child is in the process of learning to read, the condition should be handled as a monocular squint in the stage of alternating. Careful testing should be done for alternation, diplopia and blurring of the print at the near point. Patients with alternating squint, particularly of the divergent type, will frequently show poor binocular vision when they have first learned to hold their eyes straight. In several of our cases monocular vision was 6/6 in each eye, and binocular vision, a blurred 6/60. This naturally tends to discourage the child in his efforts at binocular vision, and the condition must be looked for and trained. Training is best done with a reduced Snellen chart in the stereoscope, and the patient should be encouraged constantly to use both eyes together, even if vision is blurred, and to make constant attempts to get the images clear without allowing one eye to drift out or in.

These are the factors which we have found to be detrimental to children in the first and second grades who are just learning to read. Occasionally a child will learn to read well and rapidly by the sentence method, but somewhere between the third and the sixth grade his reading ability will decrease, and he will drop back to reading by the word method. In these cases the cause is almost always fusional convergence deficiency.

DEFICIENT FUSIONAL CONVERGENCE

The first and most common result of fusional convergence deficiency is occasional monocular suppression. The left eye is the one usually suppressed in a right-handed child. Reading becomes slow and difficult because the dominant right eye reads the words first, and the left eye, usually suppressed, will have occasional flashes of vision, which cause confusion. This is particularly true when the child is reading long words or sentences. The concentration necessary to interpret the word stimu-

lates the vision of the left eye, binocular vision is momentarily restored, and the print changes in appearance or position. This necessitates rereading of the word or sentence. Children tell us that long words will frequently jump or the print become confused, and it is difficult for them to pick up the beginning of each new line of print.

The condition can be diagnosed easily and is frequently discovered by seeing one eye waver slightly during the test for the near point of convergence or by having the red line of the Maddox rod disappear occasionally during the phoria test. On the stereoscope it is easy to find by the use of the small Keystone dots, the Wells F-L or some similar test object. Watching the child read when a tiny light is reflected in the pupils gives a clear indication of frequent regressions. The ophthalmograph, which photographs the actual movements of the eyes during reading, gives an accurate record of such movements but will not indicate momentary suppression during which coordination of the eyes is not lost.

The second difficulty caused by poor fusional convergence is constant alternating at the near point. This alternating is frequently present without any measurable phoria. The eyes remain perfectly straight, but at the near point vision alternates rapidly between the two eyes. Sometimes the fusion at distance may be perfect, but usually there is occasional alternation. The condition is easy to diagnose with the stereoscope if small test objects are used at the near point.

Another type of suppression which makes a child unable to read rapidly is suppression of the periphery at the reading distance. This can be found by using the small three dot Keystone fusion test cards or the Wells ONE at the near point. As the child looks at the three dots, the center will remain fused, but the upper and lower dots will disappear suddenly and simultaneously, to reappear and disappear at intervals of a few seconds. Occasionally, with concentration on the middle dot, the upper and lower dots will disappear permanently until concentration is relaxed. Sometimes a child will volunteer the information that when he concentrates on a new or difficult word the rest of the page becomes blank or blurred. With so small a field of vision, naturally it is impossible for a child to read rapidly by scanning a sentence. He must pay close attention to each particular word or syllable.

The cause of these types of reading difficulty seems to be an improper distribution of binocular attention. It probably starts in the first or second grade as a result of refractive error, poor convergence, weak fusion or a strongly dominant eye. These factors result in an overconcentration on macular vision for the purpose of mastering print, and the attention is improperly distributed between the maculas of the two eyes or between the macula and the periphery. It is interesting to

speculate on the role of the bilateral cortical representation of the macula in these types of fusion deficiency.

It is important to point out that in testing for these fusion deficiencies the work must be done at the reading distance with small test objects, as convergence and accommodation enter into the causes, and if the testing is done at distance or with large targets the conditions will be completely overlooked.

METHOD OF CORRECTION

The first step in the correction of the difficulties of older children is careful refraction under atropine. The same low errors which cause some children in the first grade to fail to learn to read will cause older children to become poor readers when the visual demands of increased study tire or strain the eyes. The most frequent condition found in the children I have seen is low astigmatism of one eye with no astigmatism in the other or low astigmatism of both eyes at oblique axes.

The second step in remedial training is to restore normal binocular habits. This can be done most efficiently by orthoptic training. Special emphasis should be placed on near point fusional convergence, elimination of all suppression and maintenance of clear images for print. The Snellen chart reduced for the stereoscope, the Wells G series of printed cards and the Wells system of bar reading are excellent aids. The span of attention should be gradually increased by the use of more complex targets and larger lines of print, and special attention should be given to complete binocular attention during coordinate movements to the left and right.

The remaining training is in the actual process of reading and should be in the hands of a skilled teacher. Children may be divided into two main groups: children of from 6 to 8 who are failing to learn to read and children from 10 to 18 who read too slowly or with too little comprehension for their required school work.

There is a wealth of available literature on the technics of remedial training in reading, and it is not the purpose of this paper to discuss such technics except from the point of view of establishing normal ocular habits.[2] If the child has not learned to read and ocular difficulties are present, it is wise to repeat the steps used in the early teaching of reading. He should read first from charts placed from 6 to 8 feet (183 to 244 cm.) in front of the eyes (the material in such charts being adapted to his age and experience) and should advance from charts to primer size

2. Betts, E. A.: The Prevention and Correction of Reading Difficulties, Evanston, Ill., Row, Peterson, & Company, 1936. This book should be read by every one interested in reading difficulties. It contains an excellent bibliography.

print for his first efforts at book reading. Gradual reduction in the size of print should be made only when good reading habits are established for the larger types. Whether to reenforce visual images by kinesthetic images through tracing the sentences to be read is a decision which rests with the teacher. We have found it an excellent aid in cases of frequent reversals and mirror reading or writing.

In the older group of children the correction of ocular difficulties frequently leads to immediate comfort and swifter reading. If habits of word reading are too firmly established, remedial training in sentence reading is necessary. In either case the remedial steps should be followed by an assignment of much easy and interesting supplementary reading. This serves the twofold purpose of establishing the corrected ocular habits permanently and of building up a reading vocabulary made deficient by the years of slow reading.

The ophthalmologist, in his supervision of a child with a reading problem, should not lose sight of the psychologic factors which quickly enter the picture when a child fails in normal scholastic achievement. Emotional "sets" against teachers and parents, the process of reading itself and school in general are probable complications. Children who fail to read when the ocular difficulties have been corrected and there are no language or hearing complications should be referred to a psychiatrist for analysis and solution of emotional difficulties which are probably barring his progress.

Ophthalmologic Review

CARBON DISULFIDE POISONING

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One of the results of the increasing application of chemicals in industry is a widening of the field of industrial risks. Although improved methods of manufacture have eliminated many of the occupational hazards previously encountered, new ones have appeared, and some previously considered eliminated have reappeared. Such is the case with regard to carbon disulfide.

Sixty years ago the literature contained many reports of carbon disulfide poisoning occurring among those who worked with rubber. Articles to be vulcanized were passed through a solution of sulfur chloride and carbon disulfide. Changes in the method of manufacture and adequate protection of the worker have practically eliminated this source of intoxication from the rubber industry.

Today carbon disulfide is being used extensively in this country in the rayon and the transparent paper industry and to a much lesser extent in the manufacture of dipped rubber goods and water-proof cements and in certain extractive and pharmaceutic processes. Considering the tremendous increase in the production of rayon and transparent paper within the past few years, it is evident that a new source of intoxication has appeared. Carbon disulfide is absorbed chiefly through the respiratory system, though the alimentary tract and the skin are capable of some absorption. When applied to the skin in the liquid state, it causes anesthesia and then a first or second degree burn. Delpech,[1] in 1856, was the first to recognize that the signs and symptoms of carbon disulfide poisoning present a definite clinical entity. His reports are still classic, and little has been added to the knowledge of this disease since publication of his original papers. Many reports have subsequently come out in the foreign literature since then, and one report, by Gordy and Trumper,[2] was recently published in this country.

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1. Delpech, A.: Accidents que développe chez les ouvriers en caoutchouc l'inhalation du sulfure de carbone en vapeur, Union méd. **10**:265, 1856.

2. Gordy, S. T., and Trumper, M.: Carbon Disulphide Poisoning, with a Report of Six Cases, J. A. M. A. **110**:1543 (May 7) 1938.

However only one report has previously appeared in the American ophthalmologic literature: that of Heath,[3] in 1902. The frequent mention of ocular complications in all previous reports and the opportunity to examine 120 workers who had been exposed to carbon disulfide over a number of years prompted the study reported here.

In cases of severe carbon disulfide poisoning, failing vision has been reported as one of the earliest and most common symptoms. Delpech reported 15 cases of amblyopia in his series of 34 patients; Desmarres, an ophthalmologist who examined some of his patients, stated that there were no visible changes in the fundus to explain the marked reduction in vision. Shortly after this it was determined that the amblyopia was due to a central scotoma. The cases became so common that in 1885 the Ophthalmological Society of the United Kingdom appointed Frost, Gunn and Nettleship [4] to report on the ocular complications of carbon disulfide poisoning.

The scotoma is reported to be small, bilateral and central, though it frequently extends slightly to the temporal side of fixation. It varies but slightly in intensity and is practically always absolute. Terrien [5] stated that the scotoma may be large (about 30 degrees) and that it may be uniocular, but few have agreed with him. Uhthoff,[6] in his classification of toxic amblyopias, placed carbon disulfide in that group of exogenous toxins frequently associated with peripheral neuritis: He stated that besides the central defects there was at times a slight peripheral depression of the field of vision. This is substantiated in the literature and in the observations made by my associates and me. Little [7] reported a case in which there was only peripheral contraction of the field and no central scotoma, which was considered unusual. The conductivity of many of the nerve elements apparently is frequently impaired, as in many of the patients complete red-green blindness was noted.

Chromatopsia and photophobia have been noted by some patients before the marked reduction in vision. The objects appeared greenish blue or red. Just what significance this may have is hard to say; Terrien claimed that it was due to the toxic effect of carbon disulfide on

3. Heath, F. C.: Amblyopia from Carbon Bisulphide Poisoning, Ann. Ophth. **11**:4, 1902.

4. Frost, W. A.; Gunn, R. M., and Nettleship, E.: Report of the Committee on Poisoning by Bisulphide of Carbon and Chloride of Sulphur, Tr. Ophth. Soc. U. Kingdom **5**:157, 1885.

5. Terrien, F.: Deux cas d'amblyopie par le sulfure de carbone, Paris méd. **10**:317, 1920.

6. Uhthoff, W., in von Graefe, A., and Saemisch, E. T.: Handbuch der gesamten Augenheilkunde, Leipzig, Wilhelm Engelmann, 1911, vol. 11, pt. 2 a, p. 45.

7. Little, D., in Discussion of Toxic Amblyopia, Lancet **2**:18, 1887.

the visual purple. That might also explain the frequently reported symptom of night blindness.

The other ocular manifestations are likewise part of a systemic intoxication which is most evident in the central and in the peripheral nervous system. Galezowski [8] was the first to report paralysis and weakness of accommodation in these cases. This disorder has been observed several times since, though the vision was usually so markedly reduced that measurement of accommodation was impossible.

Pupillary disturbances were not constantly observed in the reported cases. The pupils were frequently dilated and reacted poorly to light. Inequality of the pupils also has been mentioned by Koelsch [9] and others. These phenomena were not always associated with amblyopia and have been known to persist after improvement in the general condition of the patient.

Only 1 case in which nystagmus occurred has been reported, that of Berbes.[10] Laudenheimer,[11] Koelsch and others mentioned that nystagmus may be present but reported no personal observations. The extraocular muscles were rarely affected, and no cases of diplopia have been reported. Bergeron and Lévy [12] were the first to draw attention to anesthesia of the cornea in these patients. They confirmed their observations on animals and noted that the corneal anesthesia appeared before that of the skin and lasted longer. They considered that it was due to the systemic effect of carbon disulfide and not necessarily to the local action of the gas on the cornea. This, moreover, was not a frequent finding in the reported cases.

Carbon disulfide may often be the cause of severe psychogenic disturbances; many cases have been reported. Of chief interest to the ophthalmologist are the patients reported by Charcot [13] and Marie.[14] Their patients had hysterical hemianesthesia, with tubular fields,

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8. Galezowski: Troubles visuels consécutifs à l'intoxication par le sulfure de carbone, Rec. d'opht. **4**:121, 1877.

9. Koelsch, F.: Handbuch der Berufskrankheiten, Jena, Gustav Fischer, 1935, vol. 1, p. 553.

10. Berbes, P.: Observation de pseudo-tabes dû à l'intoxication par le sulfure de carbone, France méd. **1**:3, 1885.

11. Laudenheimer, R.: Die Schwefelkohlenstoffvergiftung der Gummi-Arbeiter unter besonderer Berücksichtigung der psychischen und nervösen Störungen und der Gewerbe-Hygiene, Leipzig, Veit & Co., 1899.

12. Bergeron, G., and Lévy, P.: Note sur l'anesthésie de la cornée dans l'empoisonnement par le sulfure de carbone, Gaz. méd., Paris **19**:584, 1864; Compt. rend. Soc. de biol. **1**:49, 1864.

13. Charcot, J. M.: Leçons du mardi à la Saltpêtrière, Paris, E. Lecrosnier & Babé, 1889.

14. Marie, P.: Sulfure de carbone et hystérie, Bull. et mém. Soc. méd. d. hôp. de Paris **5**:445, 1888.

micropsia, macropsia and monocular diplopia on the same side as the anesthesia.

The ophthalmoscopic examination seldom revealed any changes in the fundus. There was occasionally slight hyperemia of the disk or temporal pallor. Galezowski, Baader [15] and Uhthoff are the only ones to report atrophy of the optic nerve following severe intoxication. Nuel [16] and Hirschberg [17] have reported slight stippling and pigmentation of the macula lutea.

Another ocular condition has been frequently noted among the spinning room workers in the rayon industry, though it is not definitely known how far carbon disulfide is responsible for its occurrence. The symptoms are usually photophobia, halos about lights, a feeling of sand in the eyes and finally pain and profuse lacrimation. Strebel [18] called the condition keratitis punctata superficialis traumatica. He attributed it to hydrogen sulfide, which is present in the spinning bath. Klein,[19] who examined some 600 patients, described the corneal condition as follows: First there is slight graying of the cornea; small punctate elevations then appear subepithelially and finally break down, and the cornea stains lightly. The lesions heal rapidly and do not leave any permanent opacity. The workers as a rule do not notice these symptoms until they have worked for two or three eight-hour shifts. To explain this latent period, Duke-Elder [20] advanced the theory that gases from the spinning solution sensitize the corneal epithelium to photochemical changes which would not affect the normal cornea. Most writers have expressed the opinion that the lesion is caused chiefly by hydrogen sulfide and that carbon disulfide probably plays a minor role.

MATERIAL AND METHODS

My personal observations concern the examination of 120 workers employed in a rayon industry in which the viscose process of manufacture was used. Most of them were working at the time. The investigation was part of a general medical examination; the complete results of the survey will be published in monograph form at a later date. The ocular tests included determination of

15. Baader, E. W.: An Hirntumor erinnernde Vergiftungserscheinungen durch Schwefelkohlenstoff, Med. Klin. **28**:1740, 1932.

16. Nuel, J. P.: Altération de la macula lutea, Arch. d'opht. **16**:473, 1896.

17. Hirschberg, J.: Schwefelkohlenstoffvergiftung, Centralbl. f. prakt. Augenh. **13**:268, 1889.

18. Strebel, J.: Durch SO_2 verursachte Augenschädigungen (spez. zentrale punktförmige Viskoseverätzung der Hornhäute): Schutz durch Maskenbrille mit Zinkkohlefilter, Schweiz med. Wchnschr. **53**:560, 1923.

19. Klein, E.: Les lésions oculaires dans les fabriques de soie artificielle, Arch. d'opht. **45**:686, 1928.

20. Duke-Elder, W. S.: Text-Book of Ophthalmology, St. Louis, C. V. Mosby Company, 1937.

corrected vision with pinhole; peripheral fields on a perimeter and central fields on a campimeter, stereocampimeter and Haitz charts; external examination; measurement of the near points of accommodation and convergence, and an ophthalmoscopic examination. The corneal sensitivity and pupillary reactions were checked by another observer (Dr. F. H. Lewy) with Frey's hairs and a Zeiss pupilloscope.

RESULTS

Approximately 75 per cent of those examined had some ocular complaints. They varied from the usual complaints that might be attributed to refractive errors to the definite symptoms of rayon keratitis. Two workers gave a history which suggested that transient amblyopia had occurred several years previously, but they had no evidence of it during the present examination. More than half of those examined had been employed for ten years or longer.

	Location of Workers							
	Churn Room		Spinning Room		Elsewhere		Total	
	24		84		12		120	
Ocular Defect	No.	%	No.	%	No.	%	No.	%
Diminished corneal reflex	8	33.5	54	64.0	5	41.8	67	55.0
Pupillary disturbance	15	62.5	32	47.5	1	8.3	48	40.0
Enlargement of blindspot	9	37.5	15	18.0	3	25.0	27	22.5
Field defects	4	16.5	3	3.6	1	8.3	8	6.7
Changes in disk	6	25.0	10	12.0	3	25.0	19	15.9
Vascular changes	7	29.0	24	28.5	3	25.0	34	28.4
Nystagmus	15	62.5	42	50.0	4	30.0	61	50.8

The findings are tabulated for the sake of comparison, though I realize that errors may be introduced by attempting to analyze results which involve such small figures. The churn room was considered to have the highest concentration of carbon disulfide. Those listed as working elsewhere were working in parts of the plant other than the churn room or the spinning room.

Diminution of the corneal reflex was found in over half of the workers examined; it was most common in the spinning room workers, despite the fact that all other signs were found more commonly in churn room workers. This would imply that diminution of the corneal reflex may be due in part to the same factors that produce the keratitis. Diminution of the pupillary reaction to light was the second most common finding; it was more frequently observed among the churn room workers.

Enlargement of the blindspot was not noted in any of the previously reported cases but was found in 22.5 per cent of the workers I examined. The enlargement varied from two to three times the normal size. In

a small number of cases there was a definite contraction of the peripheral field for a 1 mm. white test object.

Rotatory nystagmus was present in about half of the workers; occasionally it was evident in the primary position, but it was usually elicited only on horizontal or upward gaze.

Vascular changes, which varied from early arteriolar sclerosis to marked arteriosclerosis, were found in slightly less than one third of the cases. The changes in the disk were not marked; they varied from slight blurring to a questionable pallor of the papillomacular bundle. None of those examined showed definite neuritis or atrophy.

No workers with symptoms of rayon keratitis were seen during the course of the examination, though many of them gave a typical history of keratitis and several had been transferred to other parts of the plant because of their susceptibility to soreness of the eyes. Several of them were examined with a slit lamp, but no corneal lesions were seen, nor was there any scarring from previous attacks of keratitis.

COMMENT

Carbon disulfide is known to be an exogenous toxin producing changes in the central and peripheral nervous systems. Ranelletti [21] reported that in 80 per cent of the cases there is some evidence of neurologic disturbances. Koester [22] has shown by experimental work that the toxin produces changes in the ganglion cells of the brain and in the myelin sheaths of the peripheral nerves. Birch-Hirschfeld [23] was unable to demonstrate any changes in the ganglion cells of the retina, while Offret [24] found degenerative changes in the optic nerve.

The ocular signs of carbon disulfide poisoning are essentially those of a systemic neurologic disturbance. Though amblyopia was the symptom most frequently noted in the previously reported cases, it was not found in any of the workers in the series reported here. One patient had poor central color vision, but no scotoma was demonstrable. In all the previously reported cases the poisoning occurred in an industry in which the exposure was much greater than in the rayon industry, and the symptoms frequently developed after a short exposure. Enlargement of the blindspot has not been previously noted in the literature; this I believe to be of definite significance. It was present in 10 of the

21. Ranelletti, A.: Die berufliche Schwefelkohlenstoffvergiftung in Italien, Arch. f. Gewerbepath. u. Gewerbehyg. **2**:664, 1931.

22. Koester, G.: Ein klinischer Beitrag zur Lehre von der chronischen Schwefelkohlenstoffvergiftung, Deutsche Ztschr. f. Nervenh. **26**:1, 1904.

23. Birch-Hirschfeld, A.: Beitrag zur Kenntnis der Netzhautganglienzellen, Arch. f. Ophth. **50**:230, 1900.

24. Offret, A.: Essai sur l'amblyopie par le sulfure de carbone, Thesis, Paris, no. 455, 1906.

patients who were considered to have slight blurring of the disk margins. Depression of the peripheral field, as mentioned previously, is not an unusual finding when toxic amblyopia is associated with peripheral neuritis, as is the case with carbon disulfide poisoning.

The diminution of the light reflex, while only occasionally mentioned in all previous reports, occurred in nearly half of my cases. Two of the workers showed definite recession of the near point that was not due to presbyopia or to a refractive error.

Diminution of the corneal reflex was the most constant finding; as previously noted, it is probably due in part to the direct action of the gases and the spray from the spinning solution. In the reports on keratitis no mention was made of the corneal sensitivity, but there is probably some relation between the keratitis and the diminution of the corneal reflex.

The nystagmus I believe to be vestibular in origin. It is surprising that this has been reported only once before, while I was able to demonstrate it in over 50 per cent of the cases.

SUMMARY

I have reviewed briefly the ocular signs and symptoms of carbon disulfide poisoning and have reported on the examination of 120 workers who had been exposed to carbon disulfide for a long time. Many of them showed systemic signs of chronic intoxication. Enlargement of the blindspot I believe to be the most significant early ocular sign of chronic carbon disulfide intoxication.

A complete bibliography and correlation of these data with those of the other examiners will appear in monograph form at a later date.

Clinical Notes

HOMONYMOUS HEMIANOPIC PARACENTRAL SCOTOMA

Report of a Case

T. D. Allen M.D., and H. F. Carman Jr., M.D., Chicago

The purpose of this report is twofold: first, to contribute to the literature one more case of hemianopic paracentral scotoma and, second, to corroborate the reports of previous authors.

In reviewing the literature we found that prior to 1930 only a few cases of this type of defect of the visual field had been reported. In 1907 Wilbrand [1] reported 8 cases and described them in detail. In 1908 Posey [2] reported 1 case. Stieren [3] in 1924 found a hemianopic paracentral scotoma in a patient with an acute facial abscess in whom meningitis later developed, the scotoma appearing after development of the meningitis. Newton [4] described 1 case in 1936. O. and H. Barkan [5] reported 2 cases in 1930, and in 1935 O. Barkan and Boyle [6] presented another case. In the last account the authors summarized the clinical findings in cases in which this type of visual field defect is present. Invariably the following symptom complex is found: (1) difficulty in reading and fixation of objects located close to the central field on the side of the defect; (2) absence of reduced visual acuity; (3) characteristic changes in the visual field, namely, a homonymous scotoma that does not include the macula, with maintenance of the peripheral field so that an untouched portion of the field lies between the periphery and the scotoma, and (4) normal ophthalmoscopic findings.

The rarity of this condition is probably due to the fact that it has never been emphasized and consequently it is frequently overlooked. In the textbooks on perimetry little discussion has been devoted to this

1. Wilbrand, H.: Ueber die makulär-hemianopische Lesestörung und die von Monakowsche Projektion der Makula auf die Sehsphäre, Klin. Monatsbl. f. Augenh. **45**:1, 1907.

2. Posey, W.: Report of a Case of Right Homonymous Hemianopia in the Macular Regions, Ophth. Rec. **17**:236, 1908.

3. Stieren, E.: Central Homonymous Hemianopic Scotoma, Am. J. Ophth. **7**:764 (Oct.) 1924.

4. Newton, F. H.: Paracentral Homonymous Hemianopic Scotoma, Am. J. Ophth. **19**:600 (July) 1936.

5. Barkan, O., and Barkan, H.: Central and Paracentral Homonymous Hemianopic Scotoma, Am. J. Ophth. **13**:853 (Oct.) 1930.

6. Barkan, O., and Boyle, S. F.: Paracentral Homonymous Hemianopic Scotoma, Arch. Ophth. **14**:957 (Dec.) 1935.

type of defect in the visual field. Traquair [7] merely defined the defect. He stated:

> A hemianopic scotoma is a central hemianopia. The central field in this respect resembles the whole field in miniature, the apices only of the quadrants affected being defective. Sparing of the fixation area is uncommon in hemianopic scotoma.

Traquair's term "fixation area" is not clear. If by this he means the macular area, then all cases reported in the literature in which there were sparing of the macula and preservation of good visual acuity are in contradiction to his statement. Fuchs [8] stated:

> In the case of partial hemianopic defects the lesion has the same situation but instead of affecting all, affects only a part of the fibres running from the chiasm to the cortex on one side or a very limited part of the visual cortex itself. Such partial defects may be limited to a central or paracentral scotoma symmetrically placed in the visual field of each eye; and such defects may be central—even cortical in origin.

The present lack of knowledge concerning the anatomy of some of the visual pathways and the fact that postmortem examination has not been performed in any of these cases to date make a discussion of the location of the lesion more or less futile. We can safely say, however, that the lesion may be at the level of the lateral geniculate bodies or anywhere above that point. The etiologic factor is undetermined but probably is a vascular accident in most cases. Toxic conditions, emboli and local infective processes must be considered.

In reviewing the cases thus far reported, including the case reported here, certain definite conclusions can be drawn: 1. Homonymous hemianopic scotomas are not as rare as formerly believed. 2. This type of defect in the visual field is usually associated with a constant syndrome, namely, (*a*) sudden onset of a defect in the visual field in persons often otherwise healthy, (*b*) characteristic complaints of difficulty with reading and fixation, (*c*) normal ophthalmoscopic findings, (*d*) absence of reduced visual acuity and (*e*) good prognosis for visual acuity. 3. The cause and the anatomic changes of this condition are still matters of conjecture. 4. Homonymous hemianopic scotoma is a condition that may be easily overlooked during routine examinations unless careful attention is given to the history and a perimetric examination made of the central field. 5. The case reported here agrees in most details with the findings in those previously reported.

REPORT OF CASE

Mrs. C. B. S. aged 48 was first seen June 28, 1937. She complained of a severe generalized headache of three days' duration and difficulty in focusing objects and in reading. A few hours previous to the onset of the headache she noticed that her "right hand vision was fuzzy." She stated that she saw only

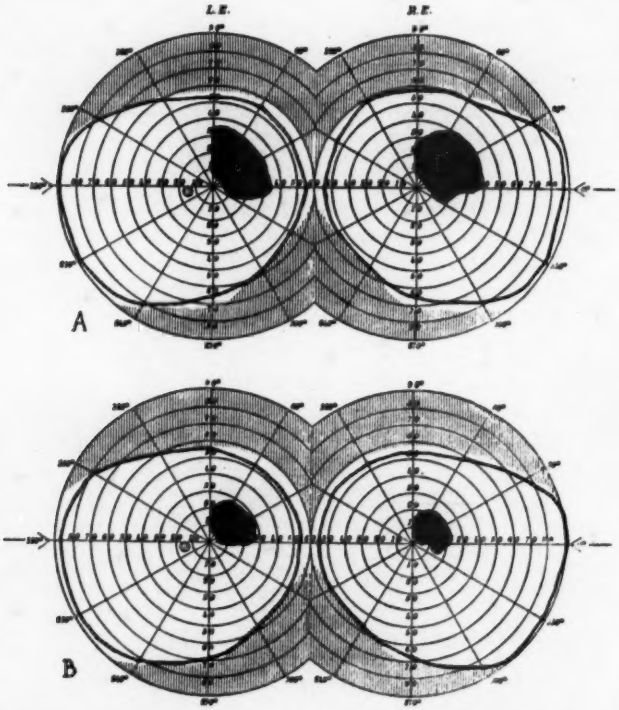
7. Traquair, H. M.: An Introduction to Clinical Perimetry, London, H. Kimpton, 1927.

8. Fuchs, E.: Text Book of Ophthalmology, ed. 8, translated by A. Duane. Philadelphia, J. B. Lippincott Company, 1924.

the left half of things. This visual disturbance persisted for a few hours and then began to clear, up so that at the time of our first examination her only visual complaints were "fuzzy" vision and difficulty in reading.

Further inquiry revealed that the patient was being treated by Dr. Harold O. Jones for uterine fibroid tumors and mild secondary anemia. Subsequently hysterectomy was performed by Dr. Jones, the cause of the secondary anemia thereby being removed. A general examination by Dr. Fred E. Ball did not reveal any other organic disturbances.

Vision in the right eye with a + 0.62 sph., + 0.38 cyl., ax. 180 was 20/20+. Vision in the left eye with a + 0.25 sph., + 0.38 cyl., ax. 170 equaled 20/20+. The near point with a + 1.25 sph. addition was 32 cm. for Jaeger test type I.



A, visual fields of patient taken on June 29, 1937, with a 3 mm. white test object at 330 cm., and an illumination of 7 foot candles. *B*, visual fields taken on April 21, 1938, with a 3 mm. white test object at 330 cm. and an illumination of 7 foot candles.

The intraocular tension in each eye was 20 mm. (Schiötz). There was no disturbance of function of either the extraocular or the intraocular muscles. The fundi were entirely normal; there were no pathologic changes in the retinal vessels, and both optic disks were of normal color and structure. The only abnormal ocular finding, except an error of refraction and presbyopia, was a right homonymous hemianopic paracentral scotoma. This defect was found on repeated examinations. Ten months after our first examination the scotoma had decreased somewhat in size. A complete disappearance is not expected and it will in all probability become stationary and permanent.

After consultation with the patient's general physician, 5 minims (0.31 cc.) of sodium iodide three times a day was ordered empirically. This was used continuously from Oct. 6, 1937, until April 28, 1938. No other form of treatment was instituted.

The prognosis in this case as in others like it is good; no loss of visual acuity is expected, and the patient should experience no visual difficulties once she accommodates herself to the presence of the blind-spot in her field of vision.

Abstracts from Current Literature

EDITED BY DR. WILLIAM ZENTMAYER

Bacteriology and Serology

ANTIGENIC PROPERTIES OF CORNEA AND VITREOUS. E. WOLLMAN, P. GONZALES and P. DUCREST, Compt. rend. Soc. de biol. **127**: 1188, 1938.

The transparent tissues of the eye, cornea and vitreous do not share the immunologic properties of the lens but react in the same way as other vertebrate tissues. Rabbit-ox antiserum precipitates suspensions of cornea and of vitreous but does not affect that of ox lens. The lens of the cephalopod, however, reacts like the other tissues of its organism.

J. E. LEBENSOHN.

Conjunctiva

ANTEPOSITIO CONJUNCTIVAE FORNICIS OPERATION IN SEVERE CASES OF SPRING CATARRH. N. I. SHIMKIN, Brit. J. Ophth. **22**: 287 (May) 1938.

The article of Shimkin is concluded with a summary, part of which is quoted here:

"The author points out that pathological investigations have shown that in spring catarrh the tarsus of the lid is quite healthy, and the affection consists in the disease of the conjunctiva and subconjunctival tissue only, in consequence of the abnormal growth of this tissue and its hyaline degeneration in the region of the tarsal conjunctiva.

"In view of the fact that the tarsus of the lid in spring catarrh is healthy, and the tarsal conjunctiva only is diseased, the author recommends careful excision of all the conjunctiva and subconjunctival tissue from the whole surface of the tarsus, beginning at the extreme lid border, and replacing it with healthy conjunctiva of the fornix. The author calls this operation 'antepositio conjunctivae fornicis,' as the conjunctiva of the fornix, separated deeply down towards the eyeball, is drawn forward on the tarsus, freed from the morbid conjunctiva and subconjunctival tissue."

W. ZENTMAYER.

LIMBIC FORM OF SPRING CATARRH. FROGÉ, POURSINES and CHINIARA, Ann. d'ocul. **175**: 236 (March) 1938.

Spring catarrh, although not rare in France, is much less frequently seen than in other regions, such as the Orient. In France this disease is not only frequent but is also a continual source of worry to ophthalmologists because of the resistance it presents to all forms of treatment. In some cases cure is spontaneous, and in others the condition seems indifferent to all therapeutic measures.

The palpebral form often coexists with trachoma and does not attract the attention of the patient as does the limbic form. On the other hand, the limbic form may exist alone without any lesion of the palpebral conjunctiva, and it is this form that the authors here describe.

Details as to the clinical and microscopic aspects are given. The authors believe it necessary to differentiate between the lesions of the adult and those of the child and the adolescent. Adults, for instance, do not show, except in exceptional cases, the considerable edema of the limbus seen in the infant and the adolescent; the bulbar lesion of the adult consists chiefly of a simple hypervascularization. Often in the adult, as pointed out by Lagrange, one finds an anaphylactic phenomenon. This is not the case in the infant. The limbic form of spring catarrh presents in the infant an ocular lesion peculiar to its age and similar to phlyctenular keratoconjunctivitis.

S. H. McKee.

Fungi in Normal and Diseased Eyes. A. Fazakas, Arch. f. Ophth. 138: 416 (Feb.) 1938.

Fazakas has made a systematic study of the fungi which can be grown from normal and from diseased eyes. The incidence of positive growth (37 per cent of all diseased eyes and 26 per cent of all clinically normal eyes) and the variety of the fungi are amazing.

P. C. Kronfeld.

Congenital Anomalies

A Case of Primary Bilateral Anophthalmia (Clinical and Histologic Report). E. Recordon and G. M. Griffiths, Brit. J. Ophth. 22: 353 (June) 1938.

The developmental anomaly reported in this article was seen in a male child. Pregnancy and labor had been normal. There was no history of a developmental anomaly in the family of either parent, and there was no consanguinity. The child died of bronchopneumonia at the age of less than 3 months. A detailed anatomic description of the brain is given. Serial sections were made of the orbits. On the left side the sections were vertical and on the right side horizontal. In both orbits the six extrinsic muscles and their nerves were found embedded in fat. On the left side, four rectus muscles were attached by their anterior end to a minute nodule of fibrous tissue containing pigment granules, apparently lying free and not containing any recognizable cell structure. The pigment was brownish and did not give a reaction to the test for iron. The nodules did not contain any trace of retinal neuroepithelium or any type of cell other than the fibrous tissue. On the right side the muscles were not attached to the fibrous mass.

The author maintains that the case is one of bilateral primary anophthalmia in which there has been an absolute failure in the development of the optic vesicles and that it is distinct from those cases of

"degenerative" or "consecutive" anophthalmia in which the vesicles appeared to have formed and subsequently to have atrophied.

The article is illustrated.

W. ZENTMAYER.

Cornea and Sclera

VITAMIN D COMPLEX IN KERATOCONUS: ETIOLOGY, PATHOLOGY AND TREATMENT OF CONICAL CORNEA; PRELIMINARY REPORT. A. A. KNAPP, J. A. M. A. **110**: 1993 (June 11) 1938.

After referring to a recent paper by Blackberg and himself in which the consistent production of keratoconus in dogs fed a vitamin D deficient, low calcium diet was reported, the author states that more recent experiments on rats have produced similar results. The results of treatment of 11 patients with vitamin D, in the form of viosterol, and calcium, in the form of mineral mixture tablets, are presented.

The author gives the following conclusions:

"A consideration of this material suggests that the calcium-phosphorus metabolism is an important factor in the development of the cornea. It would appear that the lack or deficiency of these metabolic factors would favor weakness of the membrane. This weakness then may manifest itself as a preliminary, noninflammatory ectasia of the cornea. The administration of Vitamin D and calcium in this condition has given gratifying results. In fact, the results apparently are so encouraging that it may be we have come upon a factor or the factor in the etiology of this perplexing pathologic entity. It is true that but eleven patients (eighteen eyes) with a rare condition have been treated. Still, the regular decisive improvement of all suggests that the vitamin D complex has a definite place in the therapy of keratoconus. It is hoped that further observations along this same line will serve to give a more conclusive conception of its place in our understanding and treatment of keratoconus."

W. ZENTMAYER.

Experimental Pathology

EXPERIMENTAL PRODUCTION OF LOCAL EOSINOPHILIA, PARTICULARLY IN RELATION TO SPRING CATARRH. A. KITSUKAWA, Acta soc. ophth. jap. **39**: 17 (Feb.) 1938.

In this investigation Witte peptone was given intravenously. A degree of shock was produced which resembled an anaphylactic manifestation. It is therefore believed that this peptone, as well as histamine, is important in the study of anaphylaxis.

Tests with Witte peptone were carried out in the same manner as those with egg albumin. The results were as follows: If the peptone was instilled into the eye of the guinea pig which had not been previously prepared, no changes resulted; if the animal, however, had been sensitized, the instillation of the peptone caused a local anaphylaxis in the conjunctiva.

Microscopic changes were the same as were found in experiments with egg albumin; that is, there was a fleeting edema of the con-

junctiva, and on microscopic examination local eosinophilia of the conjunctiva was found after ten and after twenty-eight hours.

ARNOLD KNAPP.

General Diseases

DISEASES OF THE EYE IN LEPROSY. P. S. RAMEYEV, Vestnik oftal. **11:** 787, 1937.

Rameyev observed among leprous patients in a leprosarium in Uzbek (Turkestan) 38 persons, or 66.6 per cent, with ocular lesions. Many cases of trachoma were found in the region, but none of the leprous patients was affected with the disease. Consequently, Rameyev believes that possibly leprous patients are immune to trachomatous infection.

The common ocular lesions associated with leprosy are discussed.

1. Madarosis, or falling of the eyelashes, is one of the first and constant signs of leprosy and is due evidently to trophic disturbance in the hair follicle. Lagophthalmos is observed in the neural form and leads to blindness, if tarsorrhaphy is not done early, before opacification of cornea sets in.

2. The sclera is affected next in frequency. The color of the lesion is violet or pale yellow. The nodules or lepromas in the sclera have a tendency to spread on the cornea and conjunctiva; the shape of the lesion is frequently triangular, with its base at the limbus.

3. The cornea is frequently involved (in about 80 per cent). The process is sluggish, without reactive manifestations, so that the patient often notices it only when the vision is impaired because of central opacities of the cornea. Ulceration as a rule hardly ever occurs.

4. Leprous iritis and iridocyclitis are frequently of a low grade, chronic, serous plastic type, with exudates which lead to early occlusion and seclusion of the pupil, if treatment is not administered at once. At times miosis and irregular pupils are noted at the early stage of leprosy. Leproma of the iris is often located at the lower part of the anterior chamber. Chaulmoogra oil acts favorably in cases of keratitis and scleritis. Surgical excision of the leproma usually gives good results.

Rameyev advocates that an oculist be present at a leprosarium or that physicians in charge should have sufficient knowledge of clinical ophthalmology in order to prevent many cases of blindness.

O. SITCHEVSKA.

Glaucoma

THE OSMOTIC PRESSURE OF THE AQUEOUS HUMOUR IN EPIDEMIC DROPSY GLAUCOMA. E. O'G. KIRWAN and S. N. MUKERJEE, Brit. J. Ophth. **22:** 329 (June) 1938.

In 1934 Kirwan showed that epidemic dropsy is the only general disease at present known in which glaucoma forms an integral part, and hence is the most important clinical lead ever presented on the pathogenesis of glaucoma. The authors have studied the osmotic pres-

sures of the aqueous humor in normal eyes and in glaucomatous eyes in cases of epidemic dropsy and give the following summary and conclusions:

"1. In epidemic dropsy glaucoma the difference between the osmotic pressure of blood serum and the aqueous humour is considerably reduced as the result of the appearance of proteins in the latter.

"2. In consequence a reshuffling of ions takes place exactly in the same direction as predicted by the hypothesis of membrane equilibrium. The concentration of chlorine ions diminishes in the aqueous humour while an increase can be observed in the serum.

"3. The evidence tends to support the view that in epidemic dropsy glaucoma the filtration of fluid into the anterior chamber takes place by the process of dialysation as usual, but that the equilibria concerned are at a level different from that of normal subjects, due probably to the altered permeability of the dialysing membrane."

W. ZENTMAYER.

Injuries

INJURIES ATTRIBUTED TO GLASSES OF AVIATORS. R. DE GAULEJAC, Ann. d'ocul. **175**: 315 (April) 1938.

The glasses of aviators are a constant cause of injury in aviation accidents. The injury may not only involve the orbit but at times the periorbital region, the nose and the neighboring sinuses. Though often superficial, the injury may affect adjacent bone, fracturing the nose and breaking into the frontal sinuses and bruising the inferior part of the orbit.

The injuries do not seem to vary with the kind of spectacles used; all seem to cause ocular injuries, orbital and periorbital and superficial and deep. In 4 of 8 recent cases of injury glass cut the tissues more or less severely, while in 3 the injuries were so severe that a detailed account of each is given.

S. H. MCKEE.

Lens

THE OCCURRENCE OF SO-CALLED DINITROPHENOL CATARACTS WITHOUT INGESTION OF DINITROPHENOL. H. BARKAN and J. W. BETTMAN, Am. J. Ophth. **21**: 165 (Feb.) 1938.

The following summary is given:

"An account has been given of a woman, 23 years old, who took a reducing agent, 'Slendrets,' for a week and lost only two pounds in weight. This preparation contained no dinitrophenol, yet the woman developed cataracts similar in every way to those we have associated with the ingestion of this drug.

"Thorough examination and history were negative except for the following data: A fractured nose, fracture of the right maxilla and the use of ergot over two years before entry; a fever of unknown etiology

one year before entry; use of quinine three months before entry; the extraction of five teeth because of apical abscesses two months before entry; and chronic pelvic inflammatory disease.

"We do not believe that the above-mentioned positive findings were pathogenic factors in this case. The cause of the patient's cataracts remains unknown. They are certainly not coincident with the taking of dinitrophenol."

W. S. REESE.

INTRA-CAPSULAR EXPRESSION OF CATARACT. C. V. KRISHNASWAMI, Brit. J. Ophth. **22:** 274 (May) 1938.

The method of expression employed by the author is a modification of the Smith procedure. Anesthesia is produced by blocking the facial and ciliary nerves. The corneal incision is a little less than half the circumference of the cornea. A conjunctival flap is formed. A radial incision is made in the iris. With the strabismus hook placed on the lower part of the cornea, gentle pressure is exerted toward the lower pole of the lens, and at the same time the bend of the hook is stroked to and fro along the lower limbus. Under this maneuver the zonule gives way at its weakest spot, which differs in different eyes. The stroking is now stopped, and the pressure alone is continued. The lens slowly expands the pupil and comes out through it, and then out of the section. The lens takes on a characteristic molding, depending on its consistency, in much of the manner of the fetal head coming out of the pelvis.

Illustrations accompany the article. W. ZENTMAYER.

THE p_H OF LENS IN NAPHTHALENE CATARACT OF RABBIT. P. REISS and J. NORDMANN, Compt. rend. Soc. de biol. **128:** 111, 1938.

In the rabbit the p_H of the normal lens ranges from 7.1 to 7.5. In lenses with naphthalene cataract the shift was toward alkalinity rather than toward acidity as expected, the p_H of mature naphthalene cataracts averaging 7.8. The anticipated tendency toward greater acidity occurred, however, when the lenses were removed in the initial stage of the disturbance, the p_H of these lenses varying from 7.0 to 7.2.

J. E. LEBENSOHN.

Lids

TRANSPLANTATIO CONCHAE AURICULAE TO CORRECT SPASTIC ENTROPION FOLLOWING TOTAL TARSECTOMY. N. I. SHIMKIN, Rev. internat. du trachome **15:** 15 (Jan.) 1938.

The author has observed 5 cases of spastic entropion following total tarsectomy of the upper lid (Heisrath-Kuhnt excision). He restores the integrity of the lid by grafting auricular cartilage. A layer about 2 cm. long, 1.5 cm. wide and 0.75 mm. thick, excised with its perichondrium conserved, is implanted in the lid through an incision 5 mm. from

the border of the lid and retained by three Snellen sutures, which pierce the middle of the cartilage and the remaining strip of tarsus and are brought out between the lashes.

J. E. LEBENSOHN.

Ocular Muscles

MUSCLE WEAKENING BY CENTRAL TENOTOMY. W. G. WATROUS and J. M. D. OLMSTED, Am. J. Ophth. 21: 182 (Feb.) 1938.

On the basis of experiments on decerebrate cats the authors present the following conclusion:

"Evidence has been presented which shows that if anything is accomplished by central tenotomy the beneficial results are due not to weakening of the hypertonic muscle through its tendon, but simply to a decrease in the mechanical advantage of the muscle acting on the eyeball through the formation of a new insertion, the result of adhesions."

W. S. REESE.

Operations

GONIOSCOPY OF THE SURGICAL COLOBOMAS OF THE IRIS. M. PUIG SOLANES, Am. J. Ophth. 20: 731 (July) 1937.

Puig Solanes discusses the theories explaining the beneficial effect of iridectomy. He concludes from a gonioscopic study in 5 cases that "(*a*) The reopening of the iridociliary angle is not necessary to the success of iridectomy in glaucoma. (*b*) The excision of the base of the iris—unless future observations show the contrary to be true—is not accomplished in the majority of cases of iridectomy. (*c*) The existence of an open angle and the perfect excision of the root of the iris do not guarantee the therapeutic success of the operation." He believes that the study of the action of surgical traumatism on the nervous system of the eye will help one to understand better the mechanism responsible for the good results in operations for glaucoma.

W. S. REESE.

A CORNEO-SCLERAL SUTURE IN CATARACT EXTRACTION: ITS TECHNIQUE AND ADVANTAGES. H. B. STALLARD, Brit. J. Ophth. 22: 269 (May) 1938.

Stallard considers among other advantages of a corneoscleral suture its value in the prevention of postoperative hyphema, whereas previous to its use this complication occurred in about 30 to 35 per cent of cataract extractions. In the present series in which a suture was used there has been no such complication. The author describes an eyeless corneoscleral needle which he has devised. The point of the needle is dipped into the anterior half of the substantia propria of the cornea at a point 1 mm. inside the limbus at 12 o'clock. The needle is made to traverse from 2 to 2.5 mm. of the cornea in a transverse direction before emerging. With the point of the needle facing in the opposite direction, the needle is then passed through the conjunctival and subconjunctival tissues and engages in the superficial layers of the sclera 1.5 mm. above

the limbus opposite the site at which the needle emerged. It passes transversely through the superficial half of the sclera for 2.5 mm. and is brought out through the conjunctiva opposite its entry wound in the cornea.

The article is illustrated. W. ZENTMAYER.

Orbit, Eyeball and Accessory Sinuses

AN ANALYSIS OF 71 CONSECUTIVE CASES OF UNILATERAL EXOPHTHALMOS. M. E. RANDOLPH, Am. J. Ophth. 21: 169 (Feb.) 1938.

This analysis confirms the view that sarcoma is the most common primary orbital tumor and indicates that the most frequent cause of unilateral exophthalmos in children is sarcoma, a rapid exophthalmos in the absence of inflammatory symptoms being strong presumptive evidence for this diagnosis. The mortality is high. Randolph cautions against the drainage of an orbital abscess secondary to infection of the adjacent sinuses until it has become localized. He mentions the transfrontal intracranial approach for deep orbital tumors, suggesting that persons with such tumors be referred to the neurosurgeon.

W. S. REESE.

LUXATION OF THE EYEBALL WITH COMPLETE RESTORATION OF ITS FUNCTION: REPORT OF A CASE. P. L. AKKERMAN, Vestnik oftal. 11: 581, 1937.

A student came to the clinic with the history of having injured the left eye, "which snapped out of the orbit" while he tried to pass a half-closed gate in the dark. The left eyeball was found lying in front of the lids, which were spastically closed. The cornea was lusterless, and the vision was limited to perception of hand movements. An attempt at reposition of the eyeball by opening the lids was unsuccessful. Akkerman did a canthotomy, and the eyeball was placed into the socket with no difficulty. Slight exophthalmos was present; the conjunctiva was torn away from the upper half of the eye; and the site of the insertion of the external rectus muscle was swollen and bleeding. On the next day the vision was 0.4; chemosis of the conjunctiva was present, but the cornea and fundus were normal. The vision was restored to normal within a week, and the motion of the eyeball was normal in all directions.

The mechanism of the luxation is discussed, and a review of the literature is given. The importance of reposition of the eyeball before the optic nerve is stretched too much is emphasized. Simple canthotomy was a useful measure in this case.

O. SITCHEVSKA.

Physiology

A PROCEDURE FOR MEASURING THE THRESHOLD SENSIBILITY OF THE RETINA. A. CHEVALLIER and H. ROUX, Compt. rend. Soc. de biol. 128: 231, 1938.

The dark-adapted subject places his head within an opaque globe lined with opaline. This acts as a diffusing screen for the feeble blue

light projected through an optical system similar to that in the photometer of Charpentier. The illumination is then steadily reduced till no sensation of light is recognized. The entire visual field is thus equally stimulated, and the findings are independent of central visual acuity. The method gives constant values and is more precise and delicate than the test with Tscherning's glasses.

J. E. LEBENSOHN.

Refraction and Accommodation

BENZEDRINE IN CYCLOPLEGIA. S. J. BEACH and W. R. MCADAMS, Am. J. Ophth. **21**: 121 (Feb.) 1938.

Beach and McAdams find that if benzedrine is used with homatropine or atropine little of the last two drugs need be used to obtain practically as good cycloplegia as when these cycloplegics are used repeatedly, and that the effect wears off much more quickly, permitting patients to use their eyes within one day after the use of homatropine and benzedrine and within from two to four days after the use of atropine and benzedrine. They favor using a 5 per cent solution of homatropine or a 1 per cent solution of atropine followed in two or three minutes by a 1 per cent solution of benzedrine and then a second instillation of the cycloplegic.

W. S. REESE.

ON A CASE OF TRANSIENT INFLAMMATORY MYOPIA. P. GORSE and R. BERGES, Ann. d'ocul. **174**: 844 (Dec.) 1937.

The term inflammatory myopia is borrowed from an article by Jean Sédan (*Ann. d'ocul.* **163**: 358, 1926) in which he presented two personal observations. Tscherning not only calls the condition inflammatory myopia but says that this high myopia, or dangerous myopia of the illiterate, is often congenital and accompanied by insidious choroiditis.

Publications by different writers are reviewed, and the following case is described. A man aged 53, of robust health, had fifteen years previously been given glasses (a —1.0 D. sph. for the right eye and a —0.50 D. sph. for the left eye). He was again seen by the authors in June 1936 for refraction. The correction consisted of a —0.75 D. sph. for the right eye and an —0.50 D. sph. for the left eye. The following September a spasmodic type of rhinitis developed, and the eyes were so red that the condition was considered an allergic conjunctivitis. At the beginning of October he returned for examination, as the rhinitis still persisted. The right eye was normal, but the left eye was still red. The conjunctiva was injected and had a granular appearance; a large area of episcleritis was also seen. A curious phenomenon was that the patient complained of colored vision, yellow to the left and blue to the right. Treatment was instituted, consisting of the use of zinc sulfite, epinephrine ointment and, after the chemosis had subsided, yellow mercuric oxide ointment.

The condition in this case resembled spring conjunctivitis with prompt localization of the inflammatory symptoms in the left eye. Because of the persistent nature of the condition, the possibility of syphilis was considered and mercurial treatment was prescribed, which was undeniably beneficial. Since then the presence of an old syphilis

has been confirmed, but this is of secondary importance, the authors' first intention being to report a study of transient myopia from phlegmasia of the ocular membranes.

S. H. McKee.

Retina and Optic Nerve

Variations in the Pressure of the Retinal Arteries and in the Capillary Pressure in Relation to Compression of the Globe. C. Gandolfi, Ann. di ottal. e clin. ocul. **65:** 841 (Nov.) 1937.

Since pressure on the eye produced various reflex vascular changes, such as the oculocardiac reflex, the author studied the effect of such pressure on the vessels of the opposite eye. The pulse and general blood pressure as well as the pressure in a branch of the central retinal artery and the pressure in the macular capillaries were recorded before compression and again after compression sufficient to elicit the oculocardiac reflex. The retinal arterial pressure was recorded by Bailliart's dynamometer, and the capillary pressure was recorded by an apparatus similar to that used by Horniker. With this the patient, while observing a lighted blue-glass screen, notes as an entoptic phenomenon the pulse wave in the capillaries of the macular region, which cease when pressure sufficient to obliterate these vessels is employed. Data obtained by the latter method are open to certain objections and cannot be obtained for all patients. Twenty normal persons were employed, most of them being from 20 to 45 years of age.

After compression of the globe, the pulse was retarded and the general diastolic and systolic blood pressure was increased from 5 to 10 mm. in most patients. The diastolic pressure in the retinal arteries was increased in 18 cases and remained the same in 2. The increase amounted to from 2 to 10 mm. The diastolic capillary pressure could be estimated in only 17 cases and was increased in 12. The increase in pressure seems to be mediated, like the oculocardiac reflex, by the trigeminal and the vagus nerves.

S. R. Gifford.

Dehydrogenating Processes in the Retina After Interruption of the Circulation. A. Ferrara, Ann. di ottal. e clin. ocul. **65:** 851 (Nov.) 1937.

The author interrupted the central retinal vessels of rabbits for periods of from fifteen to ninety minutes by a ligature about the optic nerve at its exit from the globe. The eyes were removed from seven to eleven days later, and the retinal tissue was tested by Thunberg's method for its power to reduce methylene blue, the retina of the other eye being used as a control. The change in dehydrogenative power was too slight to be considered of any significance.

S. R. Gifford.

Alkaline Reserve of the Blood in Idiopathic Retinal Detachment. A. Bucalossi, Ann. di ottal. e clin. ocul. **65:** 919 (Dec.) 1937.

The literature on the relation of acidity and alkalinity to swelling of the vitreous is reviewed. The vitreous has been found to be abnor-

mally alkaline in cases of glaucoma by some observers and has been shown experimentally to swell when its alkalinity is increased. Since a certain equilibrium must be assumed between the blood and the vitreous, the author investigated the alkaline reserve of the blood of 24 persons with idiopathic retinal detachment as compared with that of 10 normal persons. The average for the controls was 61.20 per cent, while that for the persons with detachment was 56.95 per cent. Figures of from 42 to 52 per cent were found for 8 persons with detachment, which brings the condition in these cases into the class of mild acidosis. In the cases of bilateral detachment the average value was especially low (52.40 per cent). It seems likely to the author that a low alkaline reserve is one of the factors favoring retinal detachment in certain cases.

S. R. GIFFORD.

DETACHMENT OF THE RETINA AND ACCIDENTS. W. LÖHLEIN, Klin. Monatsbl. f. Augenh. **99**: 376 (Sept.) 1937.

Löhlein undertook to formulate a clear understanding of the connection between detachment of the retina and accidents, giving especial consideration to expert testimony. Deploring the contradictory views of leading ophthalmologists, he mentions the two predominating reasons thereof: first, the diverging conceptions regarding the etiologic basis of traumatic retinal detachment and the impossibility to reenact the causative processes convincingly by experiments; and, second, the disagreement as to whether a certain trauma represents an accident in the sense of the law. Löhlein agrees with Velhagen, in whose opinion the final decision on the latter question must be left to the lawyer; the oculist may decide merely whether and to what extent the trauma may have been contributory in causing the detachment.

Taking it for granted that some injuries may lead to retinal detachment, the author describes and discusses the following types of causative injuries:

1. The first type consists of penetrating lesions of the anterior segment of the eyeball, followed by loss of vitreous and secondary traction through cyclitic hulls, and lesions of the posterior segment of the globe, causing tears of the retina and the consecutive formation of cords in the vitreous.

2. The second type consists of direct contusion of the eyeball, such as by transmission belts, footballs and tennis balls, the specific lesions caused by each being described.

3. The third type consists of indirect contusion of the eyeball by a bruise of the skull. Refuting Zur Nedden's opinion that injuries of this kind influence the interior of the eyeball only in a limited manner, Löhlein refers to gunshot wounds of the skull and face. Extensive tears of the choroid and retina resulted from indirect contusion without a lesion of the orbit. Healthy young men were knocked down by an exploding shell, receiving no direct injury but suffering a hole in the macula. A number of cases in point are cited, some of which were observed by the author. Extraordinary was the case of a healthy boy aged 16, with emmetropic eyes and no hereditary impediment. The

boy suffered a tear and detachment of the retina in one eye due to a fall on his face while walking on the street. The second eye remained intact during eight years' observation after the accident.

4. The fourth type consists of indirect contusion of the eyeball by severe concussion of the body. The mechanism of this type of injury, compared with that causing concussion of the brain, is illustrated by the reports of several cases and is affiliated in some instances with recurring detachment of the retina.

5. The fifth type consists of detachment of the retina after especially strenuous exertion of the body. This type requires great care of decision. Profuse hyperemia of the head and eyeball exists during bodily overexertion. Therefore, the difference between the pressure in the retina and the choroid and the traction of one or the other of the extrinsic eye muscles on the sclera may help in causing detachment of the retina.

In expert testimonies the following factors should be considered: the hereditary disposition to retinal detachment, the numeric distribution of detachment as to the age of the patient and the disposition of the senescent and myopic retina. The author adds his own cases to those of Vogt, Gonin and Lindner, in which irrelevant causes, such as sudden change of the gaze and forceful rubbing of the eyes, caused detachment of the retina in predisposed eyes. Löhlein adducts convincing material in disproving Zur Nedden's contention that trauma is irrelevant in the genesis of retinal detachment. Highly myopic eyes and belated detachments are given ample consideration in this connection.

The conclusion is this that outside influences, including indirect injuries, are actually an important factor in the mechanism of retinal detachment. It is the oculist's duty to evaluate the anamnestic data and the clinical symptoms in an endeavor to arrive at a just and fair decision in each individual case.

K. L. STOLL.

HARADA'S DISEASE. K. OKAMURA, Acta soc. ophth. jap. **39**: 14, (Feb.) 1938.

Okamura has observed 16 cases of Harada's disease during the past two years. He included in this series cases of the type described by Harada and by Vogt. The patients were subjected to a careful general examination, which included a roentgenogram of the chest, the red blood cell sedimentation test, a study of the blood and the Mantoux test. These tests showed that all 16 patients were tuberculous. In fact, in 13 cases tuberculous changes in the chest were apparent roentgenographically, and in the remaining 3 the Mantoux test was positive. The Mantoux test was positive in 13 cases, and in 3 cases in which it was negative definite tuberculous changes were found in the chest on roentgen examination.

The eye presented changes which were suggestive of tuberculosis, such as nodules in the iris, disseminated choroiditis, retinal perivasculitis and hemorrhages of the vitreous.

The author concludes that Harada's disease is a form of tuberculous uveitis.

Similar general changes were found in 3 cases of sympathetic ophthalmia, and the author suggests that sympathetic ophthalmia is a form of Harada's disease, with a detrimental effect on the uvea.

ARNOLD KNAPP.

Trachoma

THE MICROSTRUCTURE OF EPITHELIAL CELLS AND ITS IMPORTANCE FOR THE AETIOLOGY OF TRACHOMA. W. GRÜTER, Brit. J. Ophth. 22: 300 (May) 1938.

Grüter made the following observations in a study of trachoma and blennorrhagic conjunctivitis on examining the epithelium by vital and staining methods.

"1. The secretory granulations swell and divide in the trachomatous epithelium. This process is diffuse (both in Golgi's apparatus and in the cytoplasmic zone) or focal (hood-shaped) (osmium impregnation).

"2. The ballonet structures referred to above swell up and divide both in the zone of Golgi and in the cytoplasmic zone.

"3. The 'interior reticulated body' swells and turns cloudy (as can be seen clearly in the dark field and against the light). Typical signs of divisions then appear (fission of the polyhedral parts). An albuminous sediment forms in the honeycomb-like spaces in the polyhedral parts (visible in dark field and by eosin staining). Lastly appear fine nodules and still finer granules (like strings of pearls) on the interior reticulated body.

"The *Hood-shaped structure* (Prowaczek's bodies) are not homogeneous but consist of various partial structures:—

"(*a*) Focal proliferation of Golgi's sheath with more pronounced proliferation of the secretory granules (osmium images). These have also been described by V. Reiss (*Arch. f. Ophthal.*, 1913).

"(*b*) Interior reticulated body or partial structures protruding from under the nuclear calotte. Extremely fine nodules and granules appear (elementary bodies according to virus nomenclature).

"(*c*) Combination of (*a*) and (*b*), the reticulated body detaching itself and the inflamed Golgi sheath becoming stained with it."

In his conclusions, Grüter states: "Inflamed trachomatous epithelial cells cannot be shown to contain any granular structure of a nature different from their own, whether in the Golgi zone, the interior reticulated body as described or in the cytoplasmic zone."

The author states that he cannot claim that the various granular structures described in literature and tested by him by so many different methods are foreign substances, i. e., initial structures of a hitherto invisible disease germ in the cell. He considers the "trachoma rickettsias" described by Busacca to be inflammatory proliferations and divisions of granules which normally occur in the epithelial cells.

W. ZENTMAYER.

STUDIES ON THE PATHOGENY OF TRACHOMA. L. A. JULIANELLE, Brit. J. Ophth. **22:** 336 (June) 1938.

After a general survey of the literature on the pathogenesis of trachoma Julianelle details the work on which this paper is based. In his discussion he states:

"The accumulated studies on the aetiology of trachoma by numerous workers as well as ourselves no longer permit a reasonable rejection of the evidence that the disease is an infection in its own right without the benefit of associated factors such as constitution, nutrition, co-related infections, etc. . . .

". . . by way of summary and conclusion, it may be said that the infectious agent of trachoma is characterised by low infectivity, occasional filterability, marked tissue specialisation, ineffectual immunogenic properties, slight propagative capacity, sensitivity to physical and chemical agents, and the accompaniment of inclusion bodies. All these properties suggest the probability that the infectious agent is a virus. Whether the virus may be defined in turn as the inclusion body or its component elements remains to be proved, although the evidence available at the present time suggests this may be actually the case; whether again the inclusion body may be defined further as a rickettsia must also wait upon further investigation. In the meantime, the three concepts of virus, inclusion body, and rickettsia are not so divergent as they appear at first glance; what differences each appears to have from the others are of the order less of fact and more of definition and classification."

W. ZENTMAYER.

SUBCONJUNCTIVAL AUTOHEMOTHERAPY IN COMPLICATIONS OF TRACHOMA. E. SELFA MARTINEZ, Rev. internat. du trachome **15:** 87 (April) 1938.

With the idea of stimulating the local defensive mechanisms in pannus ulcer and trachomatous keratitis, the author injects 0.5 cc. of the patient's own blood in the superior cul-de-sac. The reaction is minimal, and marked improvement is generally observed within forty-eight hours. Nine cases are reported. This method has been extended to the treatment of pneumococcus hypopyon keratitis with equally encouraging results.

J. E. LEBENSOHN.

Tumors

THE ANAPLASTIC OR DIFFERENTIATED GLIOBLASTOSPONGIOBLASTOMA OF THE RETINA. G. FAVALORO, Ann. di ottal. e clin. ocul. **65:** 881 (Dec.) 1937.

The classification of retinal tumors is discussed on the basis of modern knowledge as to the histiogenesis of the various cells in the central nervous system and the types of neoplasm derived from them. Reasons are given for considering previous classifications unsatisfactory. The author reports his observations in 3 cases in which the clinical picture of so-called glioma retinae was present. Special stains, especially glial stains, showed that all 3 neoplasms were composed of

glia, but with the predominant cells in different stages of differentiation, producing three quite different histologic pictures.

In 1 case the predominant cell was the small round cell, with scanty protoplasm and without prolongations. This is the type of cell which was formerly confused with that of the small round cell sarcoma. By its staining properties, however, and the detection of a few cellular spines, it may definitely be classed as an anaplastic or undifferentiated glia cell.

In a second case the cells were pleomorphic, differing greatly both in size and in shape, being bipolar, unipolar, pyramidal, elongated and irregular, with and without processes. These must be considered as typical or atypical spongioblasts. The cells of the rosettes seen in this and in similar tumors are spongioblasts of the ependymal series, which show a tendency to unite in circles, as do the spongioblasts about the neural canal. They have nothing to do with the neuroepithelial layer, and hence the term neuroepithelioma is a misleading one.

In a third case the cells were of various sizes, more or less irregularly rounded, with cellular processes which were short and spinous or long, anastomosing with each other to form a true neuroglial reticulum. These are spongioblasts of the astrocytic series, cells more highly differentiated than the two types just described. A fourth type of glia cell, the astrocyte, was not found in these tumors, but has been described in retinal tumors by Greef, Ascunce and others.

The author criticizes the common use of the terms retinocytoma and neuroblastoma because it has not been demonstrated that embryonal retinal or neural cells are present in the usual types of retinal tumor. He would separate the gliomas, including nearly all of the retinal neoplasms described, sharply from the neuroblastomas, it being doubtful if true examples of the latter type have been seen in the retina.

He proposes a classification of the gliomas on the basis of the types of cell present. Many tumors show different zones, in each of which the predominant cell is different. He distinguishes six types of cell: (1) the anaplastic glioblast (common); (2) the spongioblast of the astrocytic series (less common); (3) the spongioblast of the ependymal series (very common); (4) the glioblast, with many processes forming a netlike or asteroid syncytium (common); (5) the highly fibrillar glioblast, highly differentiated, with fibers united in bundles (rare); and (6) the astrocyte (not common).

On the basis of this classification, the tumor in the first case would be described as a spongioependymofibrillogliobla stoma; that in the second case as an anaplastic, differentiated ependymoglioblastoma, and that in the third case as an ependymospongioglioblastoma. The commonly malignant course of the retinal neoplasms is due to the common preponderance of the anaplastic, undifferentiated cell type.

A bibliography and 21 illustrations accompany the article.

S. R. GIFFORD.

TUMOR OF THE LID IN A CASE OF BOURNEVILLE-PRINGLE'S DISEASE. E. PURTSCHER and J. WENDLBERGER, Arch. f. Ophth. **138**: 388 (Feb.) 1938.

The term Pringle's disease is used to designate the cutaneous manifestations of tuberous sclerosis of the brain (Bourneville-Hartdegen's

disease). The authors report a case of tuberous sclerosis in a girl of 9 years. In addition to other typical cutaneous manifestations of this disease, a fibroma-like tumor was removed from one upper lid. Histologically, the tumor consisted of multiple small cysts, each of which contained one or several hair shafts. The cysts had probably originated from hair follicles. The deeper layers of the tumor consisted of imperfectly developed hair follicles, and in that portion of the tumor in an early stage of development there were arrested hair follicles. The authors therefore recommend the name "follicle-nevus" for this growth.

P. C. KRONFELD.

Uvea

CHRONIC CELLULAR INFILTRATION OF THE UVEA IN SEPTIC ENDOPHTHALMITIS OF ECTOGENOUS ORIGIN. H. D. LAMB, Am. J. Ophth. 21: 137 (Feb.) 1938.

Lamb discusses the histologic changes following penetrating injury, operation or corneal ulcer. After an examination of 32 eyes he found the most characteristic change of septic endophthalmitis to be the large number of polymorphonuclear leukocytes along the inner surface of the ciliary body and in the anterior part of the vitreous. In each of these eyes there were macrophages or exudative cells of chronic inflammation in the anterior and posterior vitreous and in the anterior chamber. There was in every case a chronic factor which tended to intensify as the original virulence of the etiologic toxin weakened.

W. S. REESE.

HEREDITARY CHORIORETINAL DISEASE. M. SCHUTZBACH, Arch. f. Ophth. 138: 315 (Feb.) 1938.

In a German family of 28 members belonging to 5 different generations, Schutzbach found 18 cases of obviously hereditary chorioretinal disease which occurred in two forms, viz., as progressive atrophy of the choroid leading to typical choroideremia or as a "pepper and salt" fundus without pronounced atrophy of the choroid. The formed type occurred only in men, and the latter, chiefly in women. The relation between these two types was not clear. The assumption is plausible that they represented different stages and degrees of the same disease. The optic nerves and the retinal vessels remained normal in each type. The mode of inheritance was probably of the dominant type. The question of sterilization of the male members in whom the disease was definitely progressive was considered.

P. C. KRONFELD.

Therapeutics

RELIEF THERAPY ("ENTLASTUNGSTHERAPIE") FOR TABETIC OPTIC ATROPHY. A. MIKLÓS, Arch. f. Ophth. 138: 219 (Dec.) 1937.

The literature on the pathogenesis and the treatment of tabetic optic atrophy is reviewed. During the last ten years the disease seems to have become milder and less rapidly progressive. Lauber and Sobański believe that the course of tabetic optic atrophy is principally dependent on the

retinal circulation, that is, on the relation between the diastolic pressure in the retinal arteries and the intraocular pressure. With the dynamometric method, Lauber and Sobański have found the diastolic pressure in the retinal arteries to be so low in many cases of tabetic optic atrophy that chronic decompensation of the retinal circulation must have been present. The two authors have, therefore, recommended that tabetic optic atrophy be treated by relieving the circulatory decompensation (relief therapy, or *"Entlastungstherapie"*), that is, that therapeutic measures be employed which tend either to raise the blood pressure (tonics, caffeine and food rich in proteins) or to lower the intraocular pressure (pilocarpine or cyclodialysis).

Miklós has tried this form of treatment on a large number of patients and reports his results. He comes to the conclusion that there is a definite relation between the diastolic blood pressure and the course of tabetic optic atrophy. If the blood pressure remains abnormally low for a certain length of time, central and peripheral vision decrease rapidly. If the blood pressure rises or remains stationary at the normal or at a higher level, the vision remains stationary or decreases slowly. Tonics and caffeine, though generally ineffective as pressure-raising agents, are harmless and because of their possible usefulness are indicated in tabetic optic atrophy. Pilocarpine is, as a rule, equally ineffective as a pressure-lowering agent. In only a few cases did it lower the intraocular pressure by from 7 to 10 mm. of mercury. Cyclodialysis is the most effective pressure-reducing procedure. "The ideas of Lauber and Sobański have . . . proved correct. The method of relief therapy combined with antisyphilitic treatment is worth trying."

P. C. KRONFELD.

SUCCESSFUL HYPERTHERMIC TREATMENT OF OPHTHALMOBLENNORRHEA BY THE APPLICATION OF A STEAM SPRAY: REPORT OF CASES. I. BRECHER, Klin. Monatsbl. f. Augenh. **99**: 301 (Sept.) 1937.

Brecher reviews the modern literature on regional hyperthermy as a therapy for ophthalmoblennorrhea. He refers to Wessely, who devised the original apparatus for the application of the "steam treatment" to the eye. Brecher obtains a constant temperature of 42 C. with his method, used at a distance of from 10 to 12 cm. from the eye. The virulence of the germs was destroyed without any adverse effect on the ocular tissues. Good results were obtained in 5 adults and 13 infants. The method is of great help in those cases in which the protein therapy is contraindicated. The treatment also relieved the pain and was of eutrophic value in cases in which there was complicating corneal involvement.

K. L. STOLL.

Society Transactions

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PARKER HEATH, M.D., Detroit, *Chairman*

Eighty-Ninth Annual Session, San Francisco, June 15-17, 1938

DERRICK VAIL, M.D., Cincinnati, *Secretary*

NATURE OF THE FILTRABLE AGENT OF TRACHOMA. DR. PHILLIPS THYGESON, New York, and DR. POLK RICHARDS, Albuquerque, N. M.

This article appeared in full, with discussion, in the October issue of the ARCHIVES, page 569.

SCLEROMALACIA PERFORANS: REPORT OF A CASE IN WHICH THE EYE WAS EXAMINED MICROSCOPICALLY. DR. FREDERICK H. VERHOEFF and DR. MERRILL J. KING, Boston.

This article will be published in full, with discussion, in a later issue of the ARCHIVES.

PATHOLOGIC CHANGES IN AMBLYOPIA FOLLOWING TRYPARSAMIDE THERAPY. DR. P. J. LEINFELDER, Iowa City.

Many instances of acute loss of vision have been observed after treatment with tryparsamide, but microscopic examinations of the eyes or optic pathways of persons so affected have not been reported. Reports of pathologic studies of the eyes and optic nerves of 2 persons in whom amblyopia developed after the administration of sodium arsanilate are available in the literature. A tabetic man aged 55 received an injection of 1 Gm. of tryparsamide. Acute loss of vision was noted in forty-eight hours, which rapidly progressed to blindness. Death from uremia occurred nine days after the injection. A complete postmortem examination was made, and the eyes, optic nerves, tracts, lateral geniculate bodies and occipital cortex were removed for microscopic study. Acute degenerative changes were observed only in the ganglion cells and inner nuclear layer of the retina.

DISCUSSION

DR. FREDERICK C. CORDES, San Francisco: Of particular interest to me was the fact that examination of the occipital cortex, lateral geniculate bodies, optic tracts and nerves failed to reveal any evidence of acute inflammation or degeneration. The changes in the optic nerve were those of an old process, easily accounted for by the preexisting atrophy of the optic nerve. The changes noted in the retina have been observed in cases of acute poisoning from methyl alcohol, ethyl alcohol, quinine, nicotine and sodium arsanilate. According to Igersheimer's work, the last-mentioned drug also attacks the neuroepithelial layer.

Lillie and others have contended that the occasional reported cases of tryparsamide amblyopia have been primarily the result of an idiosyncrasy to the drug. The fact that 1 Gm. produced such marked changes would tend to confirm this opinion. I should like to emphasize again the necessity of caution in the initial doses so as to detect any sensitivity to the drug.

Clinical observation has shown that aside from the subjective symptoms the earliest changes are those of a contracted field and microscopic changes in the optic disk. The fact that the greatest changes were found in the periphery of the retina and that no acute changes were found in the optic nerve emphasizes the importance of careful studies of the visual fields early in the course of therapy. Such studies will help to detect the occasional sensitive patient.

Dr. Max Fine, San Francisco: It is unfortunate that the picture in Dr. Leinfelder's case was somewhat confused by the presence of early atrophy of the optic nerve. There is general agreement, however, that tabetic atrophy of the optic nerve begins in the intracranial portions of the nerve. The absence of extensive atrophy in the presence of marked degenerative changes in the ganglion cell and inner nuclear layers suggests that the process involved is one other than tabetic atrophy of the optic nerve. A striking feature of the sections Dr. Leinfelder has exhibited is the relative integrity of the central portion of the retina and the progressively severe changes as the periphery is approached. These findings correspond in a rough manner to the peripheral constriction of the visual field in cases of tryparsamide amblyopia. I should like to ask Dr. Leinfelder whether in the study of his specimens he was able to find a difference in the extent of degeneration in the nasal and temporal halves of the retina. Such a finding would substantiate the clinical observation of relative sparing of the temporal field, which is an almost constant feature of tryparsamide amblyopia.

The delayed appearance of atrophy of the optic nerve in tryparsamide amblyopia, even when the changes in the visual field are severe, fits in with Dr. Leinfelder's suggestion that the degeneration occurs first in the inner nuclear layer.

The question of the specific cause of tryparsamide amblyopia, the chemical group responsible and the reason why only 1 of 10 persons who receive the drug have ocular complications would appear to hinge on a factor either of idiosyncrasy or of a defective excretory mechanism. The occurrence of over 90 per cent of reactions with the first five injections speaks against a cumulative effect in the ordinary sense. Young and Meuhlenberger have shown through studies of urinary arsenic that whereas a great majority of persons excrete 95 per cent of the arsenic within twenty-four hours, a small number excrete the drug much more slowly, and in 1 instance arsenic was recovered from the urine after three weeks. It is possible that in such a person a sufficiently high concentration of the toxic agent is maintained in the susceptible tissues for a sufficiently long period to cause damage, while in the average person the same concentration may be reached but does not act over as long an interval. Studies in this direction should yield valuable information.

Dr. John Weeks, Portland, Ore.: The only experiences that I have had with amblyopia due to the use of arsenical preparations in the

treatment of syphilis were with 2 cases of syphilis of long standing. I regard the use of tryparsamide as something that should be undertaken only after careful tests have been made of the patient's sensitivity to the drug. There is rather a widespread opinion that whenever there is any atrophy of the optic nerve or any disturbance of the fundus from syphilis, tryparsamide should not be employed. I cannot speak positively in regard to that.

It is curious that the periphery of the retina should be so much more profoundly affected than the region of the macula. Amblyopia due to tryparsamide corresponds to some extent to that due to quinine, but tryparsamide has caused total blindness to persist in a few cases. No case of complete permanent blindness from quinine is on record so far as I have been able to discover.

Dr. Frederick H. Verhoeff, Boston: At present it seems to me to be of no practical importance whether tryparsamide or other arsenicals in producing blindness affect primarily the optic nerve or the ganglion cells, but it is of great scientific interest and may become of practical importance.

I have not the slightest doubt that Dr. Leinfelder has shown in this case that the ganglion cells were markedly affected. I do not feel sure that the ganglion cells were primarily affected. It seems to me, in spite of the fact that histologically there is no evidence that the nerve fibers were primarily affected, that it is possible that they may have been affected to such an extent that as a result the ganglion cells would show changes, because any injury to the nerve fibers may also injure the ganglion cells.

As I say, this is not important at present, but it may become very important. I think that it is a question that arises constantly in regard to judging the effect of toxic agents on the optic nerve and retina. Frequently one cannot determine whether it is the ganglion cells or the optic nerves that are attacked primarily.

Dr. P. J. Leinfelder, Iowa City: Dr. Verhoeff's question concerning whether the ganglion cells or the nerve fibers were primarily affected can, I think, be definitely answered. Although neurohistologic technic is by no means infallible, research that I have done with the optic nerve has shown me conclusively that if the optic nerve is sectioned or injured, pathologic changes are observable on staining with osmic acid or by the Marchi method as early as three days after the injury. Furthermore, the neurofibril will be disintegrated, not in three days, but within ten days.

It is striking that in this case there was aboslutely no evidence of acute degeneration in the nerve fiber of the optic nerve even close to the eyeball.

Dr. Sharpe brings up the question of pupillary reactions. It has been conspicuous in the literature that pupillary reactions are at first retained in spite of the subjective blindness.

Correction of Ptosis by Attachment of Strips of Orbicularis Muscle to the Superior Rectus Muscle. Dr. John M. Wheeler, New York.

This article will be published in full, with discussion, in a later issue of the Archives.

THEORY AND USE OF CROSS CYLINDERS. DR. EDWARD JACKSON, Denver.

The cross cylinder planned for optical theory was not practically useful. Made to fit physiologic, psychologic and clinical conditions, it furnishes the best method of detecting and measuring astigmatism. Reversal in two positions shows astigmatism present or absent. The direction of its principal meridians is to be fixed first, and after that, the amount of astigmatism. The technic consists of holding the cross cylinder in the right position and reversing its meridians so that the patient can tell which way is best. A cylinder placed in the trial frame is to be turned or its strength changed until the best vision is obtained and any further change makes it worse. After the approximate correcting cylinder is reached, any further change makes vision worse. When the right cylinder is thus found, the strength of the spherical lens is to be varied to find the strongest convex lens and the weakest concave lens that will give the best vision. Optical theory, or experiments with cylinders, will show the reason for each step in such testing.

DISCUSSION

DR. CHARLES K. MILLS, Woodland, Calif.: Concerning my experience with the cross cylinder, I find that the test for the axis is practically foolproof, and when it is properly performed the patient will invariably select the correct axis; but great care must be exercised in making the test for strength or the patient's interpretation may introduce errors and lead one astray.

DR. WILLIAM H. CRISP, Denver: The cross cylinder may be thought of as asking one of two questions: How much cylinder, and in what direction? The test for strength adds or deducts a cylinder of the same denomination as that before the patient's eye and gets the patient to say whether more letters are legible one way or the other. This test does not indicate just how much is to be added or deducted but merely shows that addition or deduction is to be made.

The test for axis offers two new axes and determines whether the patient wishes his lens turned in the direction of one or of the other. This test again does not immediately furnish an exact indication of how far the axis is to be moved but only that it is to be moved.

In each case the information is to be completed by making an arbitrary change of strength or axis of the kind indicated, and then the test is to be repeated until the point is reached at which no further change is demanded.

As to the problem whether to rely on the astigmatic measurements obtained under cycloplegia or those obtained after the pupil has returned to its normal size, I doubt whether one can safely dogmatize. I believe that in the majority of cases it is at least as safe if not safer to accept the astigmatic findings obtained under cycloplegia; for my own experience appears to indicate that in the majority of cases the brain has learned to select a certain limited area of the pupil and to disregard the peripheral zone when the pupil is dilated.

DR. JOHN GREEN, St. Louis: The axis of the measurable astigmatism is more accurately determined by the cross cylinder than by astigmatic charts.

I am being rather dogmatic about this because these are the rules that I have laid down for my own guidance and my associates' guidance.

In determing the axis with the cross cylinder, keep the patient in a slight fog. This should be done whether or not the patient is under cycloplegia.

When the actual test is being made, admit to the patient that for the moment you have intentionally blurred his vision. Acknowledge that in neither position of the cross cylinder will the letters be crystal clear. "There are degrees of blurring. Neither side of this glass is good. Choose the lesser of two evils."

In determining the axis for astigmatism between 0.5 and 1 D., the most useful cross cylinder is the 0.37. In determining the axis for astigmatism under 0.5 D., the most useful cylinder is the 0.25.

In using the cross cylinder for strength, the sphere should be reduced to eliminate all fog. The most useful cross cylinders are: (1) for astigmatism between 0.5 and 1 D., a 0.25 cross cylinder; (2) for astigmatism between 0.25 and 0.5 D., a 0.12 cross cylinder; (3) for astigmatism under 0.25 D., a 0.06 cross cylinder.

The 0.06 cross cylinder suggested by me ten years ago is in daily use and has been found indispensable for low degrees of astigmatism. With astigmatism under 0.5 D., this very weak cross cylinder will usually, at least for the observant patient, cause a reversal in distinctness of the Lancaster single cross lines or the triple barred cross of the Thomas chart.

VISUAL ACUITY: ITS RELATION TO FORM SENSE AND THE APPLICATION OF THIS RELATIONSHIP TO MEDICOLEGAL PROBLEMS. DR. ALBERT C. SNELL, Rochester, N. Y.

A misunderstanding of the nature of the Snellen formula expressing visual acuity is responsible for much confusion in medicolegal cases. Visual acuity means sharpness of vision, Snellen's *Sehscharfe*. Sharpness is not a function of vision; it is not the form sense but a quality of the form sense. The form sense is properly measured by visual acuity tests which determine the size of the visual angle. From the principle of the "minimum separable" there is evolved the resolving power of the detail of the form sense, a visual function. The resolving power of an eye for all degrees of acuity can be determined mathematically. The principles as set forth in the report of the Committee on Compensation for Eye Injuries are scientific. Their general adoption by all states would remove much present confusion and establish a uniform method for evaluating visual disabilities.

DISCUSSION

DR. D. F. HARBRIDGE, Phoenix, Ariz.: If it is impossible to follow all the gyrations of this subject which Dr. Snell has gone through, one should remember the constant which he and his associates have evolved, that is, 0.83625. That is really the essence of the whole subject.

The report of the American Medical Association, adopted in 1925, as presented in the paper under consideration, represents much of the personal work and research of the essayist. The soundness of the method has been proved since the adoption of the report and is subject to no further challenge. The more the method is studied and applied, the

more one is convinced of its soundness. Experiment and experience covering many years were necessary to evolve the system delineated in the paper presented. All ophthalmologists do not come into contact with cases of industrial compensation, but those who do readily admit of the practicability of the method propounded in determining the visual efficiency of the patient whose ocular function has been disturbed by injury.

In 1926 Arizona created by law its present Industrial Commission and attending system of compensation. I was again afforded the opportunity of advising in the situation, whereupon I recommended the report of the American Medical Association to the Industrial Commission as a proper method for determining awards in cases of ocular injury. The adoption of the report by the commission maintains today.

For states not yet having adopted this report as a basis for awards in cases of ocular injury, local medical associations could likely bring about such an adoption by the appointment of a committee of ophthalmologists. In Arizona the state medical association annually appoints an Industrial Relations Committee of five physicians or surgeons to serve the Industrial Commission in an advisory capacity, especially as relates to debatable injuries and compensation. The commission has been most receptive to the suggestions and recommendations of this medical committee since its inception. The Arizona State Supreme Court has commended and upheld the position of this medical committee in its relation with cases of compensation through the Industrial Commission of the state. Arizona holds a unique position in nationwide industrial circles as regards this medical committee. States still not having adopted the report might consider similar contacts through their respective medical associations in bringing about a recognition of the method described.

DR. RALPH O. RYCHENER, Memphis, Tenn.: One cannot avoid speculation when after the adoption of such an excellent report as that prepared by the Committee on Compensation for Eye Injuries one finds that there remain 23 states which have no legal schedule or method whereby visual losses may be computed. The question naturally arises as to why there should be such delay in protective legislation.

Organized labor, as a rule, affords the impetus for new laws relating to the protection of workmen, but this particular subject had never before been brought to the attention of the labor unions in Memphis. The local president proved to be intensely interested in my inquiry and has written me that he believes this schedule should be incorporated in the Workmen's Compensation Act and that he is preparing for legislation to that effect. The fate of such legislation will likely depend on the interest which ophthalmologists exhibit in explaining the benefits of such legislation to workmen and legislators who do not readily understand the technical phrases of the committee's report.

On the other hand, casualty insurance companies are not particularly interested in the adoption of such schedules but probably will not vigorously oppose them. The earnings of such companies are greater in the states under the old common law than in the states in which workmen's compensation acts are in vogue, because although higher losses are suffered in individual cases in the first groups, the rate of insurance

is increased sufficiently to make a handsome profit possible. I am assured, however, that the companies welcome a definite and fixed schedule for visual loss which will enable them to rely on definite appraisals of disability rather than on the opinions of several medical men, no two of which may be in accord as has been the case in previous litigation.

DR. WILLIAM H. CRISP, Denver: A number of states have tables which do not correspond to those of the American Medical Association as started by Dr. Snell's committee. About twenty years ago I was asked by the state of Colorado to prepare a table of this type. The best thing I could find at that time was the Chapman table of Wisconsin. I studied this table as I thought out carefully what the compensation was going to be in cases of extensive injury in which there were the average chances of diminished functional efficiency. It seemed to me the Chapman table was more generous than that of the committee of the American Medical Association and was not quite as good as it should be, and I slightly stressed those figures. The modified Chapman table has been in use by the state of Colorado ever since.

EXPERIMENTAL HYPERTENSION: VASCULAR CHANGES IN THE EYES. DR. JOHN E. L. KEYES and DR. HARRY GOLDBLATT, Cleveland.

This article appears in full, with discussion, in this issue, page 812.

FUSIONAL MOVEMENTS: ROLE OF PERIPHERAL RETINAL STIMULI. DR. HERMANN BURIAN, Hanover, N. H.

Studies concerning fusional movements of the eyes have been carried on by stimulating the central or central and peripheral parts of the retinas. No special investigations of the importance of the peripheral parts of the retinas alone in the production of fusional movements of the eyes have been made. Such a study is presented based on experiments with the aid of an arrangement which allows stimulation of any desired area of the two retinas with identical images, the size and form as well as the relative position of which can be controlled. The apparatus consists of projection lanterns and polarizing material. Fusional innervations to the extrinsic muscles result whenever peripheral stimuli fall on noncorresponding areas and the resultant relative vertical, lateral and cyclic movements of the eyes are in the direction of the displacement of the stimulated areas and are of almost the same amount, depending on the size of the stimuli and their distance from the fovea.

DISCUSSION

DR. AVERY M. HICKS, San Francisco: Under ordinary conditions of seeing, nearly all movements of the eyes are the result of images falling on a peripheral area of the retina. A subconscious stimulus is initiated in the sensory apparatus which mediates an innervation to the motor apparatus to produce the ocular movements which bring the two focal areas in alinement with the point of fixation. The character and degree of these movements depend on the location and the disparity of the areas stimulated. These movements of fixation are of such com-

mon occurrence that one hardly stops to consider the complex physiologic and psychologic acts involved.

Hofmann and Bielschowsky investigated the nature of the involuntary movements of fusion. They found (1) that these movements could not be voluntarily started, accelerated or retarded but were produced only by unusual external conditions; (2) that the movements developed gradually and that the maximum deviation could be obtained only if the external condition continued to exist for a period of time; (3) that the absolute maximum limit obtained in a series of tests could not be increased to any great extent by long, continued practice but that this limit could be reached in a shorter time after practice, and (4) that after removal of the cause of the unusual innervation which produced the movements of fusion, the fusion innervation so incited did not disappear immediately, and this temporarily prevented the eyes from returning to their usual position of rest.

Dr. Burian has shown experimentally that the fusion movements resulting from the stimulation of peripheral area of slight disparity initiate movements of the eye which in general follow the foregoing fundamental laws.

Dr. Walter H. Fink, Minneapolis: Dr. Burian stated that his work adds to ophthalmic knowledge a new function of the peripheral portion of the retina. I do not believe that this is correct, because the fusion value of this portion of the retina has been recognized for some time. Lloyd recognized this fusion power and utilized it in his stereocampimeter when he designed charts to stabilize fixation by stimulating both foveal and peripheral fusion. The value of peripheral fusion has also been demonstrated in cases of bilateral macular defects, and its power has been employed in maintaining parallelism. It has been utilized also in stimulating binocular single vision. Through the stimulation of the perpiheral fusion, binocular unity results and assists in breaking down macular suppression. In testing duction power, better stability and uniformity of readings are obtained when the target used stimulates both the macular and the peripheral portion of the retina.

One must, in considering the relative power of foveal versus peripheral fusion, keep in mind certain aspects of the physiology of the retina. Certain factors are known to weaken macular fusion and give greater fusion power to the periphery. For example, a moving object from the side will exert an attraction on the central visual area which is imperative and sets in motion a reflex act. It is generally conceded that the macula does not function well when it is moving or when the object observed is moving. One's impressions depend on a constant movement of fixation. Also, foveal fixation is momentary, and if prolonged attention is forced, it fatigues easily, with a lowering of the fusion power. Macular fusion is weakened in dim light and a central scotoma is present, whereas the perimacular portion of the retina is most sensitive. The summation of peripheral stimuli has a weakening effect on foveal fusion. The rate of movement is an important factor in peripheral fusion, and a large object, if introduced slowly into peripheral vision, may remain unnoticed. It is therefore evident that the physiology of the retina is complex, and under certain conditions the impulse of peripheral fusion is greater than that of foveal fusion. It is, however, difficult to conceive that under every day conditions peripheral stimuli which are

introduced, eliminating motion as much as possible, will exert enough influence to disrupt macular stereoscopic vision.

Dr. Hermann Burian, Hanover, N. H.: In answer to Dr. Fink, I should like to make a few general remarks. In making the quantitative experiments with the squares and the test lines, the central fusion was entirely eliminated. I did not use anything other than test lines. I have shown the mean deviations with which these experiments work, and the settings I have made myself in their accuracy, and I think that this accuracy is sufficient proof that the elimination of the central fixation has not done any harm to the experiments.

Postoperative Complication of Cataract Operations. Dr. Conrad Berens and Dr. Donald W. Bogart, New York.

On the basis of a study of the postoperative complications occurring in 1,004 cataract extractions performed at the New York Eye and Ear Infirmary during the last two years and a review of the incidence, cause, prevention and treatment of these complications, we believe that the percentage which result in blindness or impaired vision can be reduced. Complete preoperative studies, combined with careful operative technic and postoperative treatment, will often prevent serious complications after the extraction of cataract.

DISCUSSION

Dr. Watson W. Gailey Jr., Bloomington, Ill.: A close analysis of the postoperative complications described by the authors is interesting in that it shows that the percentage of loss of vitreous is practically the same with both intracapsular and extracapsular extraction.

A poor incision in which the iris is involved or one which is made too deep, including the sclera, is certainly conducive to hyphemia. It is not out of line to suspect that too much pressure in making fixation or too much pressure in dislocating the lens could be responsible for choroidal or retinal detachment or even an expulsive hemorrhage. Closure of the wound with sutures, preferably corneoscleral, has been a great step forward in the prevention of postoperative prolapse.

My personal experience has been that prolapse of the iris occurs more frequently in cases in which intracapsular extraction is done than in those in which capsulotomy is performed. The majority of my prolapses have occurred on the fourth or fifth day. The large ones are repaired by excision and are covered with a Kuhnt flap. The small ones respond excellently to the application of trichloroacetic acid after the method of the late Harold Gifford. It is wise to wait, if possible, until the eye is white when dealing with small prolapses.

I have also found that hyphemia is encountered more frequently in cases of diabetes and in cases in which the iris is very rigid and in which it is difficult to dilate the pupil. It has been my observation that hyphemia appears more frequently when a full iridectomy has been performed than when either peripheral iridectomy or iridotomy has been done. Any efforts I have made to control the occurrence of hyphemia have been fruitless. I am inclined to believe that retrobulbar injections of procaine hydrochloride combined with epinephrine hydrochloride may be responsible for the incidence of intraocular bleeding.

Dr. Joseph L. McCool, San Francisco: Many of the postoperative complications which follow cataract extraction are the result of inadequate preparation of the patient from the psychic standpoint and of accidents which may occur during the operation.

If the surgeon will take the time and trouble to explain something of the procedure to the patient and assure him that nothing he may do at the time of operation will mitigate against a successfull result, he will be agreeably surprised to find the operative risk much better than he had anticipated. To be sure, any one of the barbiturates given in adequate doses and long enough before the operation to obtain their maximum effect will add much to the success of the operation.

For more than fifteen years I have used a deep orbital injection of a solution of procaine hydrochloride and epinephrine hydrochloride in every operation in which the eyeball is to be opened. I use 1 cc. of a 4 per cent solution of procaine hydrochloride and 1 drop of epinephrine hydrochloride in a dilution of 1:1,000. I have never had any reason to regret doing so, and on innumerable occasions have been thankful that I used it.

I am willing to admit that this method does cause hypotony, but never marked nor enough to mitigate against the success of the extraction. It will and frequently does cause a slight weakness of the inferior rectus muscle but as the eye is controlled by the suture of the superior rectus muscle, this weakness is of no importance. I have never been able to convince myself that it was responsible for undue bleeding after operation. On the other hand, its advantages are many and valuable. The iris is so completely anesthetized that an accidental nicking of this membrane in making the incision causes no sensation or reaction on the part of the patient. It follows, therefore, that the subsequent manipulations of this membrane are painless, and whether one does a peripheral or a full iridectomy, it can be accomplished painlessly and with deliberation. If there is a moderately rigid sphincter and peripheral iridectomy is done, unless the iris is completely anesthetized there is some discomfort as the emerging lens slowly stretches the sphincter. The subsequent toilet of the wound is facilitated by the adequate anesthesia and can be performed carefully and thoroughly, some of the complications incident on this part of the operation thereby being avoided.

Dr. E. C. Ellett, Memphis, Tenn.: Opinions seem to differ in regard to the bad effects of focal infections on the prognosis of an intraocular operation, but personally I am convinced of their importance, especially as regards the teeth. Other important matters are complete anesthesia and akinesia. For the past year I have been using retrobulbar injections with increasing satisfaction. They overcome spasm of the rectus muscles better than any other method, but on account of interference with downward rotation a stitch under the superior rectus muscle is frequently necessary.

The advantages of a sufficiently large corneal incision and a free capsulotomy have been emphasized, and I heartily agree with what was said about the advantages of a conjunctival flap and some form of suture. The latter permits a safe and leisurely toilet of the wound, removal of lens matter, clots and bits of capsule and reposition of the iris and smoothing out of the conjunctival flaps. Sutures will not prevent prolapse of the iris, but they will limit its extent and make the

excision of a prolapsed iris infinitely safer and easier than it would otherwise be. I think that the best time to deal with this complication is as soon as it is discovered. Delay only means more trouble. Small prolapses and ectasia of the wound are well met by the application of trichloroacetic acid, as Barkan has described. If akinesia makes closure of the lids difficult, they should be closed by a stitch or by fixing the lashes of the upper lid to the cheek with collodion, as suggested by Gill. The intracapsular operation is a most valuable contribution to cataract extraction, but it is not always advisable or possible.

VASCULAR OBLITERATION FOR VARIOUS TYPES OF KERATITIS: ITS SIGNIFICANCE REGARDING NUTRITION OF CORNEAL EPITHELIUM. DR. TRYGVE GUNDERSEN, Boston.

This article will be published in full, with discussion, in a later issue of the ARCHIVES.

MIXED TUMORS OF THE LACRIMAL GLAND. DR. THEODORE E. SANDERS, St. Louis.

This article will be published in full, with discussion, in a later issue of the ARCHIVES.

VERNAL CONJUNCTIVITIS. DR. HAROLD F. WHALMAN, LOS ANGELES.

Vernal conjunctivitis is a chronic hyperplastic condition of the conjunctiva manifesting itself in many forms. The simplest is the smooth form in which the conjunctiva is slightly thickened and pale and the entire palpebral surface is involved. In some of these cases the bulbar conjunctiva adjacent to the fornix appears pale and thickened. The follicular form possesses all the characteristics of the simple form and, in addition, there are numerous small, round, discrete nodules. In the vegetative form the conjunctiva has the appearance of a greatly thickened, warty mass.

Bulbar involvement in my experience frequently has accompanied involvement of the lid. It has been observed that the bulbar conjunctiva may have the appearance of a smooth, milky thickening; follicles may appear on it, or actual vegetations may be found near the limbus.

From an etiologic standpoint there appears to be good evidence for a constitutional factor as well as for an external one, the former preparing fertile soil for the reception of the latter. Fifty per cent of all patients in my experience gave a personal history of allergy. Another 20 per cent gave an immediate family history of allergy.

The treatment of vernal conjunctivitis has been unsatisfactory as far as accomplishing a complete rehabilitation of the tissues to a normal state. Relief from symptoms can be obtained with a variety of solutions, and in my experience these tend to be on the acid side. Acetic acid, 0.25 per cent, gives relief in some cases. More effective than this is a phosphate buffer of p_H 6.6 instilled several times a day, as suggested by Hosford. Trichloroacetic acid painted on the everted and cocainized lids reduces the size of the cobblestones and aids in the relief of symptoms. Solid carbon dioxide has a similar effect. Radium is effective, but one should hesitate to use radium in cases of involvement of the limbus

in which the eyeball cannot be protected. Simple excision of the giant forms is rapid and effective. A useful procedure in the vegetative type is the utilization of an elliptic mucous membrane graft from the lip. Tests for specific allergins and subsequent desensitization have proved of little value.

DISCUSSION

Dr. M. N. Beigelman, Los Angeles: As Dr. Whalman pointed out, vernal conjunctivitis is quite prevalent in southern California. I have at present on file records of 120 cases of this disease observed in a total of about 15,000 clinical and private patients, which constitutes an average of 8 to 1,000. This rather high incidence may be partly due to the fact that for a number of reasons I was interested in the milder forms and in the earlier stages of vernal catarrh. In this respect a great deal must be added to the classic conception of the disease. Textbooks, old and new, describe vernal catarrh in the familiar terms of cobblestone granulations on the tarsal conjunctiva and of gelatinous formations on the lids. These changes, as a matter of fact, are characteristic of the advanced, final stage of vernal conjunctivitis.

Dr. Whalman spoke about the allergic aspects of vernal catarrh, and particularly about the results of desensitization, in a rather reserved tone. I fully share his attitude. True, there are some well known facts, the eosinophilia, a positive allergic history, concomitant diseases of the upper part of the respiratory tract and cutaneous lesions, which link vernal catarrh with so-called allergic diseases. Among these allergic conditions, vernal catarrh, however, occupies seemingly a special place, first, because of its histologic picture and, secondly, because of its response, or rather lack of response, to desensitization.

I have compared sections of conjunctiva from more than 30 patients with vernal catarrh with sections of mucosa taken from the nose and the accessory nasal sinuses of allergic persons. The latter specimens were obtained through the courtesy of colleagues in the ear, nose and throat department of the Los Angeles County General Hospital.

In going over the slides, one cannot help being impressed with the fact that one is dealing with two fundamentally different types of tissue reaction. Whereas the mucosa of the upper part of the respiratory tract of allergic persons is almost always edematous, often to a considerable extent, one fails to find evidence of edema not only in specimens obtained from patients with advanced fibrosed vernal catarrh but in those obtained from patients with the disease in the earliest stages. I have sent, over a period of years, 11 patients with vernal catarrh to competent allergists for treatment. I am sorry to report 11 failures.

Certain analogies between vernal conjunctivitis and established allergic disease, as was stated before, cannot be denied. They should be considered, however, as a starting point for future investigation rather than as a closing answer to the complicated problem of vernal catarrh.

Dr. Albert N. Lemoine, Kansas City, Mo.: Early in my work on allergy I immunized about 15 patients with the pollens to which they were found to be hypersensitive. This immunization was done in the latter part of the winter before the time for the onset of the attacks, and all of the patients were much improved or completely relieved for the first year; but the second year there were varying degrees of recur-

rences, and for the third year most of the patients were found to be practically not benefited at all. This is quite in line with other artificial immunization; that is, it is only temporary in a majority of the cases.

I was impressed with Dr. Whalman's advice to use a buffer solution slightly on the acid side. This has a scientific basis and should be beneficial. For the same reason I have used an ointment containing 10 per cent citric acid once or twice daily. When it is to be instilled once daily, it is preferable to use it at bedtime. When it is used twice daily, the second instillation should be given in the morning. I have found that it greatly benefits most of the patients; in fact, I have found that it relieves the itching and sticky, rubbery discharge and reduces the size of the vegetation more than any other form of treatment I have used. In my opinion, alkaline buffer solutions as suggested by some authors are contraindicated. In the past I have used an alkaline buffer solution with no noticeable results.

TREATMENT OF CANCER OF THE EYELIDS. DR. GEORGE S. SHARP, Pasadena, Calif.

The treatment of cancer of the eyelids is primarily one of irradiation. The lethal or cancerocidal dosage is calculated according to the histologic type and dimensions of the growth. The irradiation is delivered by an external source, such as a radium plaque, or by interstitial means, such as radium needles or radon seeds. Frequently the combination of external and interstitial irradiation may be adapted for the best permanent result. Forty-eight patients with cancer of the eyelids were treated from 1932 to 1937 inclusive and biopsy gave positive evidence of cancer in all instances. The follow-up study has included 92 per cent of the patients. Many have not yet lived five years after treatment, but all have lived more than one year, and there has been no evidence of recurrence or complicating deformity in the group.

DISCUSSION

DR. EVERETT L. GOAR, Houston, Texas: For many years it has been my custom to refer all patients in whom I suspected a malignant lesion of the eyelids to a dermatologist for treatment. I do not believe that treating these lesions surgically serves the best interest of the patient. It is true that these growths can be removed safely and surely by wide excision, by cautery or by fulguration, but the loss of tissue and subsequent scarring is undesirable. Many a patient has been subjected to a plastic operation on the eyelid that would not have needed it if the neoplasm had been treated by radium.

Having referred these patients for treatment, it was necessary for me to turn to the consultant, Dr. C. M. Griswold, for information, and he has furnished me with statistics of patients treated by him during a ten year period. His records show 208 patients with cancer of the eyelids, 136 of whom were males and 72 of whom were females. As to location, 100 of the growths were at the inner canthus, 24 were at the outer canthus, 68 were in or near the central area of the lower lid and 16 were in or near the central area of the upper lid. Five of the patients were under 30 years of age, but the vast majority were 50 or over. While biopsies were not done for every patient, Dr. Griswold

estimates that about 5 per cent of the growths were of the squamous cell type, while 95 per cent were of the basal cell or basal squamous cell type.

All the patients were treated by topical applications of radium, with an average per patient of 550 milligram hours. There were 8 failures in the series. Most of the remainder of the patients have been followed for a varying period of from one to ten years, and their lesions are satisfactorily healed. Cicatricial ectropion has not occurred as a complication from the treatment, but in 5 patients in whom the lesion had perforated the lid and the conjunctiva was involved, symblepharon developed. No irradiation cataract has been noted in the series. All patients had a permanent loss of lashes on the affected lid.

Dr. Griswold has used the same technic throughout the series. A 2 mm. lead mold, which is wrapped in pure gum rubber to prevent secondary irradiation, is placed between the radium and the cornea. The radium plaque, encased in a 0.5 mm. platinum shield, is applied directly to the lesion. Three or four applications are made within a week. In the majority of cases in the early stages this has caused the lesion to disappear within six or seven weeks, leaving a thin, pliable scar that is scarcely visible.

Dr. Dohrmann K. Pischel, San Francisco: Many ophthalmologists have felt that when possible surgical excision of small epitheliomas was the simplest and quickest method for dealing with such tumors. If the growth is small, this method appears to me to be correct. If the surgical procedure is properly planned and executed, no deformity will result, and it is true that convalescence is short and comfortable. However, the small lesions that are amenable to surgical treatment are also most amenable to irradiation, and I personally feel that irradiation is the method of choice for such radiosensitive tumors, as Dr. Sharp has described.

Unfortunately, these cancers are most often seen when in a late stage, and here surgical treatment is impossible. It is therefore interesting to see the excellent results which can be achieved by radiation therapy. It must, of course, be emphasized that such excellent results are not to be obtained by careless work.

An Operative Procedure for Glaucoma of Shallow Chamber Type: Multiple Excisions of the Root of the Iris and Deepening of the Anterior Chamber. Dr. Otto Barkan, San Francisco.

This article will appear in full in a later issue of the Archives.

Sulfanilamide Treatment of Trachoma: Preliminary Report. Dr. Fred Loe, Rosebud, S. D.

In August 1937, 2 patients at the Rosebud Indian Hospital who had had trachoma, one for eighteen months and the other for two years, were selected for treatment with sulfanilamide. Both patients had been treated with grattage followed by the administration of silver nitrate intermittently during the period of their infection, with no noticeable improvement. On the basis of their body weight they were given ⅓

grain (0.02 Gm.) of sulfanilamide, with an equal amount of sodium bicarbonate, per pound of body weight daily for ten days. Then the dose was decreased to ¼ grain (0.016 Gm.) of sulfanilamide a pound daily for fourteen days. No other medication was allowed during this period. Within five days after treatment was begun changes in the conjunctiva were observed; the redness gradually disappeared, the granules and papules decreased in size and the blood vessels became increasingly visible. With a maintenance dose of ¼ grain of sulfanilamide a pound daily, the two patients were apparently cured of trachoma within one month.

After the aforementioned dose of sulfanilamide was used in the treatment of 140 patients with trachoma, the following conclusions were made as to improvement:

Improvement of subjective symptoms consisted of cessation of lacrimation within twenty-four hours, loss of photophobia within twenty-four hours and improvement of vision within seventy-two hours in cases of pannus. Improvement of objective symptoms included paling of the conjunctiva and paling of the trachomatous patches and flattening of the granules and follicles. In the cases in which there had been no scarring from instrumentation, the conjunctiva apparently resumed its normal velvety texture at the end of two months. The blood vessels of the conjunctiva became more visible on the fifth or sixth day of treatment, and daily thereafter they became more normal. In 30 cases of pannus in which treatment was given in the hospital it was noted that the opacity began clearing between the eighth and the fifteenth day, depending on the density of the pannus, with great improvement of vision. The granules on the lower lids were found to be the last objective symptom to disappear.

DISCUSSION

Dr. Harry S. Gradle, Chicago: Stimulated by the original report of Dr. Loe to the Department of the Interior on the effects of sulfanilamide on trachoma among the Indians, I started treating a series of patients with the drug. Twenty-five persons were selected from the patients in the Trachoma Clinics of Southern Illinois, where all are outpatients, and 16 from those of the Illinois Eye and Ear Infirmary, all of whom remained in the hospital. The types of trachoma were distributed as follows:

Stage	Trachoma Clinics	Infirmary	Total
I	1	0	1
IIa	8	1	9
IIb	6	2	8
IIIa	6	7	13
IIIb	4	1	5
IV	0	5	5
	25	16	41

Of this group of patients, 5 were forced to discontinue the drug within a few days because of systemic symptoms that ranged from mere headache and nausea to actual cyanosis, necessitating digitalis. The patients at the Illinois Eye and Ear Infirmary were followed by laboratory study daily, with the following findings: (*a*) Bacteriologically, organisms were found in only a few cases. (*b*) The hemoglobin

showed a fairly uniform decrease of from 10 to 15 per cent. (*c*) The red cell count showed no change except for a moderate decrease in isolated cases. (*d*) The white cell count showed a fairly uniform decrease of from 1,000 to 3,000 cells.

Summarizing the impressions gained from three weeks' observation of these patients, who did not receive any local treatment except a cleansing wash with physiologic solution of sodium chloride, the following seemed to be the salient features:

1. Those with trachoma of stages II and III responded fairly uniformly in a most surprising fashion in that the velvety patches and hypertrophy disappeared rapidly. The thickened and hyperemic conjunctiva became thinner and pale, the individual vessels became visible, and the secretion disappeared in the majority of instances. The results of three weeks of treatment with sulfanilamide approximated those with from three to six months of local treatment, although there was no scar formation.

2. Regardless of the stage of trachoma, photophobia and lacrimation disappeared rapidly. This subjective improvement was most striking and, to the patients, most gratifying.

3. Persons with trachoma of stages IIb, IIIa and IIIb showed marked improvement in vision when the vision was decreased due to pannus. In cases in which the trachoma was of longer duration and of the malignant type or in which there were corneal scars due to old ulcers the amount of visual improvement was negligible. In some instances the visual results were almost miraculous.

4. Persons with trachoma of stage IV and of stage IIIb in the malignant form showed practically no improvement.

So, taken by and large, it would appear that in the use of sulfanilamide one has a new means of combating trachoma in the acuter stages. The drug is not without danger and should be taken only when medical observation is possible every twenty-four to forty-eight hours. Apparently children and persons of the older, plethoric type do not tolerate it as well as others. How efficacious it is in stage I, I have no means of knowing, nor is it known yet how lasting are the improvements noted. In a year from now Dr. Hirschfelder, Dr. Ackerman and I will report on these same patients, who will have no local treatment in the meantime, unless an exacerbation should occur.

At this point it seems most appropriate to give all credit and priority to Dr. Loe, who conceived the idea, and to the Indian Medical Service, which made it possible for him to try it out on a large scale.

News and Notes

SOCIETY NEWS

Treacher Collins Prize.—Under the title Treacher Collins Prize the council of the Ophthalmological Society of the United Kingdom has instituted a prize of £100 to be awarded triennially for the best essay submitted on a subject selected by the council.

The prize is open to qualified medical practitioners of any nationality, but the essay must be written in the English language. The subject for the first award of the prize is "Cerebrospinal Disease and Its Relation to the Optic Nerve."

The closing date for sending in essays for the first award is Dec. 31, 1938. They should be submitted to the honorary secretary, Ophthalmological Society of the United Kingdom, 5, Racquet Court, Fleet Street, E.C.4, from whom also any further particulars can be obtained. No name should be on any essay, but a distinguishing pseudonym or quotation, which should also be on a sealed envelop containing the candidate's name and address. This envelop should accompany the essay.

Société d'ophthalmologie de Paris.—The annual meeting of the Société d'ophthalmologie de Paris will be held on Nov. 20, 1938. The following addresses have been announced:

Dr. Lhermitte will speak on the pathology and pathogenesis of softening of the brain.

Dr. Magitot will speak on the society, from its foundation to the present day.

The principal report will be delivered by Dr. Dubois-Poulsen, on so-called hypertensive retinitis.

Formation of the American Orthoptic Council.—On Oct. 11, 1938, a group of ophthalmologists met in Washington, D. C., and organized the American Orthoptic Council.

Three members had been appointed for this purpose by each of the three national ophthalmologic societies as follows: for the American Ophthalmological Society, Dr. John Dunnington, Dr. Alfred Cowan and Dr. Edwin Dunphy; for the Section on Ophthalmology of the American Medical Association, Dr. Derrick Vail, Dr. Everett Goar and Dr. Harold Gifford; for the American Academy of Ophthalmology and Otolaryngology, Dr. LeGrand Hardy, Dr. Grady Clay and Dr. Avery Prangen.

The following officers were elected: president, Dr. LeGrand Hardy; vice president, Dr. Derrick Vail, and secretary-treasurer, Dr. Edwin Dunphy.

It was voted that this council be known as the American Orthoptic Council and that its function shall be the regulation of the principles and practice of orthoptic training. The following resolutions were adopted. 1. Orthoptics has a definite place in ophthalmology. 2.

Ophthalmologists should know more about this subject. 3. Ophthalmologists in general are unable to carry out this work themselves, and therefore technicians are needed. 4. The national societies through the American Orthoptic Council should take over the training of technicians, and a central station should be established for training of such technicians.

By-laws were adopted which provide that the council shall be composed of nine executive members, three from each national society, and three associate members, who shall be orthoptic technicians or instructors, to be selected by the nine executive members. It was also provided that examination shall be held at least once a year and that a certificate of proficiency shall be awarded to those candidates who have satisfied the board of examiners. A set of rules governing the training and practice of orthoptic technicians and a code of ethics governing deportment of such technicians were also adopted.

A syllabus for student orthoptic technicians will be issued shortly.

Obituaries

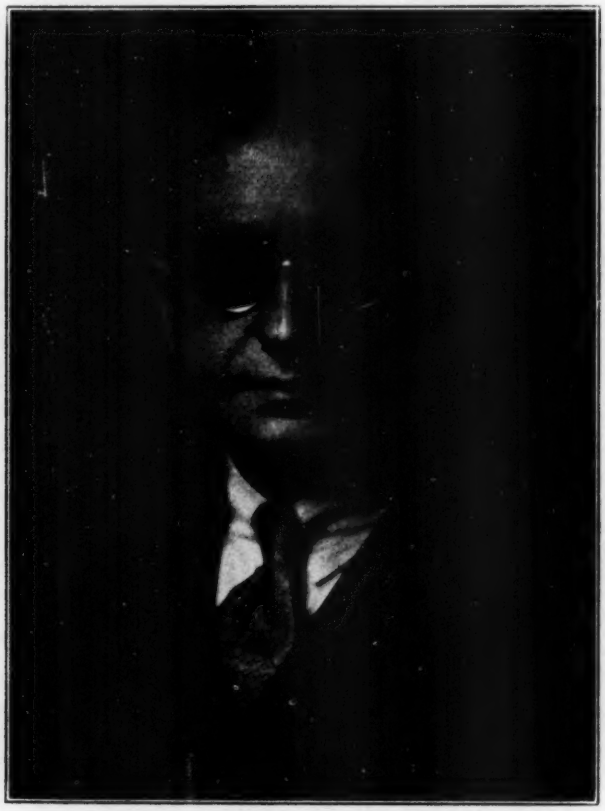
JOHN MARTIN WHEELER, M.D.
1879-1938

John Martin Wheeler, son of Henry Orson Wheeler and Elizabeth Lavina (Martin) Wheeler, was born on Nov. 10, 1879, at Burlington, Vt. He was a descendant of Thomas Wheeler, of Cranefield, Bedfordshire, England, who came to America with his wife, Anne Halsey, and settled at Concord, Mass. His father, a lawyer, was superintendent of schools at Burlington for thirty-three years. His early education was obtained at the public schools in Burlington, after which he entered the University of Vermont, receiving the degrees of Bachelor of Arts in 1902, Doctor of Medicine in 1905 and Master of Science in 1906. He served his alma mater as instructor in anatomy in 1906 and 1907, during which time his first scientific contributions were published, on "The Viability of Typhosus Bacillus Under Various Conditions."

Becoming interested in ophthalmology, he secured an internship at the New York Eye and Ear Infirmary, from which he graduated in 1908. He began the practice of his specialty in New York in 1909, in association with Dr. D. W. Hunter, a connection he maintained until Dr. Hunter's retirement in 1917. He was actively identified with the New York Eye and Ear Infirmary for many years. He served that institution with true devotion in all capacities. He was first an assistant surgeon and then senior assistant surgeon in the clinic of Dr. John E. Weeks until 1919, when he was appointed an attending surgeon. He was a member of its board of directors and a consulting surgeon at the time of his death. In addition to this active connection, he was associated with the Bellevue Hospital and the Fifth Avenue Hospital for many years. He was visiting surgeon in charge of the ophthalmic service at the Bellevue Hospital from 1925 until 1928, when he resigned to accept the directorship of the ophthalmic service of the Presbyterian Hospital. At the time of his death he was director of the Institute of Ophthalmology, Presbyterian Hospital, and consultant ophthalmologist to the following hospitals: The Bellevue Hospital, the New York Eye and Ear Infirmary, the Fifth Avenue Hospital, the New York Post-Graduate Medical School and Hospital, the Neurological Institute of New York, the Sloane Hospital for Women, the Babies Hospital, the Psychiatric Institute, St. Luke's Hospital, of Newburgh, N. Y., and the Hackensack (N. J.) Hospital.

The knowledge he gained from this wide clinical experience enabled him to speak authoritatively on all phases of ophthalmology. His inquisitive mind spurred him on to learn everything possible from every case. He was a keen diagnostician, whose sound judgment and practical suggestions made him a most helpful consultant.

As an undergraduate teacher he was an instructor in ophthalmology at Cornell University Medical College from 1911 to 1915 and professor



JOHN MARTIN WHEELER, M.D.
1879–1938

of ophthalmology at New York University from 1921 to 1928, at which time he resigned to accept a similar professorship at Columbia University. While he was greatly interested in seeing that his medical students acquired a sound practical knowledge of ophthalmology, his real interest lay in postgraduate instruction. After many years of postgraduate teaching at the New York Eye and Ear Infirmary, where his courses on surgery attracted students from far afield, the ideal of his life was realized in the opening of the Institute of Ophthalmology

in 1932, with him as its director. Although the acceptance of this new position necessitated the giving up of a large private practice at great personal sacrifice, he gladly did it because of his love for postgraduate teaching. He then began to devote the greater part of his time to the training of his residents and staff. His tireless energy, his wise and sympathetic counsel and his genuine sincerity made him an ideal leader. His quiet unassuming manner endeared him to all. His rounds and seminars were occasions never to be forgotten by his associates.

He entered the medical corps of the army during the World War as a captain, with an assignment to the air medical service. After a comparatively short time he was transferred to Fort McHenry, Md., where he was placed in charge of the ophthalmic service. This was an active hospital post filled with disabled veterans who required all sorts of reconstructive surgical treatment. Here was his long-looked-for opportunity to learn all he could about plastic surgery; so with great enthusiasm he began this new work. His thorough knowledge of anatomy and sound surgical judgment combined with his ingenuity and diligent work soon won for him a national reputation as a plastic surgeon. He loved the intricacies of a difficult plastic problem and derived great satisfaction from its successful completion. He reported this army experience before many medical meetings and with great modesty received the acclaim of the ophthalmologic world.

He was not a prolific writer, contributing only about 50 articles to the ophthalmic literature, but whatever he wrote was well done. He had no use for mere words, so his articles were always brief and to the point, at the same time being clear and explicit. His writings were largely on surgical procedures. In 1915 he wrote the chapter on "Eye Surgery" in Johnson's "Operative Therapeusis." His thesis for the American Ophthalmological Society, in 1916, was entitled "A Study of Hemorrhage into the Anterior Chamber Subsequent to Operations for Hard Cataract." He has written a number of well known articles on plastic surgery.[1]

In addition to these plastic procedures, he reported on an opening for secondary cataract by a single straight incision and iridotomy by

1. Wheeler, J. M.: Free Dermic Grafts for the Correction of Cicatricial Ectropion, Am. J. Ophth. **3**:251-255, 1920; War Injuries of the Eyelids: Plastic Operations For a Few Types, Arch. Ophth. **49**: 35-42, 1920; Restoration of the Margin and Neighboring Portion of the Eyelid by a Free Graft from the Lower part of the Eyebrow and the Skin Directly Below It: Report of an Illustrative Case, J. A. M. A. **75**:1055-1057 (Oct. 16) 1920; Restoration of the Obliterated Eye Socket, Am. J. Ophth. **4**:481-488, 1921; Correction of Cicatricial Ectropion by Use of True Skin of the Upper Lid, J. A. M. A. **77**:1628-1631 (Nov. 19) 1921; The Use of the Epidermic Graft in Plastic Eye Surgery, Internat. Clin. **32**:359-370, 1922.

the same method, at which time he described a useful discission knife which bears his name. He then became interested in exophthalmos and published several excellent articles on this subject. As his presidential address before the American Academy of Ophthalmology and Otolaryngology in 1934, he outlined the duties of the ophthalmologist toward the blind in a sane article entitled "Blind People." In the same year he reported before the American Ophthalmological Society an ingenious method of advancement of the superior oblique and inferior oblique ocular muscles. His later writings were on new operative procedures for the correction of spastic entropion and ptosis, and his last article was entitled "The Use of the Orbicularis Palpebrarum Muscle in Surgery of the Eyelids."

He was actively connected with many medical societies, being a member of the American Medical Association, the American College of Surgeons, the American Ophthalmological Society, the American Academy of Ophthalmology and Otolaryngology (past president), the Society of Plastic and Reconstructive Surgery (past president), the Medical Society of the County of New York, the Medical Society of the State of New York, the New York Academy of Medicine and the New York Ophthalmological Society. Although a regular attendant at the meetings of most of these organizations, he often had little to say, for with characteristic shyness he used to remark "I came to learn, not to talk." For many years he was a member of the editorial staff of the *American Journal of Ophthalmology*. He was also one of the founders of the newly created American Board of Plastic Surgery.

He was twice the recipient of an honorary degree of Doctor of Science, the first degree being conferred on him by the University of Vermont in 1928, while Middlebury College paid him a similar tribute in 1933. In 1931 he was decorated Commander of the Order of the Crown of Siam in recognition of the services he had rendered its ruler. In 1936 he received the Leslie Dana Medal for "his outstanding achievements in the prevention of blindness and the conservation of vision." He served seven years as a member of the directorate of the National Society for the Prevention of Blindness.

In 1912 he married Julia Warren Smith, of Burlington, Vt., who survives him along with their four children, Martha, Charles, Edward and Ann. Dr. Wheeler was a devoted husband and father, spending most of his spare time with his family. He shunned society and loved the peace and quiet of home life. His family and his work were his great interests, and he found little time for golf, art and music—his hobbies.

As a man, he was quiet and unassuming, carrying his great honors with extreme modesty. In his work, he was painstaking and thorough.

His perseverance and determination were never better shown than after the loss of his left eye from a sarcoma of the choroid in 1935; he continued to operate with his usual skill and dexterity. To him this catastrophe was a challenge, which he bravely accepted and conquered. This incident best bespeaks the character of John Martin Wheeler, who died at his summer home in Underhill Center, Vt., on Aug. 22, 1938. In his death, ophthalmology has lost one of its truly great men, for he was not only a highly successful practitioner and dextrous surgeon but a true friend, an inspiring leader, a great teacher and a sympathetic and wise counselor.

JOHN H. DUNNINGTON, M.D.

In the spring of 1907, Dr. John Wheeler, then a teacher in the department of anatomy of the Medical School of the University of Vermont, came to the New York Eye and Ear Infirmary, with an introduction from the executive surgeon, the late Dr. Richard Derby, and it was my duty as resident in ophthalmology to entertain him. From that time an intimate friendship was formed. Dr. Wheeler became a member of the house staff in 1908; as an intern he was conspicuous for his diligence, and even then his dexterity as an operator attracted attention.

As most men are largely guided by their preceptors, I have always felt that the meticulous care in plastic operations shown by the late Dr. Dwight Hunter and the exquisite operative skill of Dr. John E. Weeks, both of whom were then surgeons at the Eye and Ear Infirmary, must have had a profound influence on Dr. Wheeler, for it was in ophthalmic surgery that he particularly excelled.

In addition to the professional attainments of Dr. Wheeler, which are so well known to the world of ophthalmology, the personal side of this man was impressive. He endeared himself, both to doctor and to patient, by his calm, quiet and unobstrusive manner. He shunned publicity and disliked the notoriety of the press which so often comes to men of prominence. His interest in the young doctor was never failing, and some day these men will proudly say that their success was due to his material assistance and guidance.

As head of the Institute of Ophthalmology of Columbia University, it was not only his demand that his associates should be capable and that the institution should function as an efficient place of learning but also his great ambition that there should ever be a spirit of sympathy, kindliness and friendliness. And such was the life and character of its chief. He was a practical Christian, charitable and constantly doing good.

After his tragic operation three years ago, his determination and will to adjust himself quickly were a marvelous display of courage, and to his intimates there seemed, as one expressed it, "the rebirth of a man."

The passing of John Martin Wheeler ended the beautiful life of "A Great Physician."

While it is a gigantic undertaking, it is hoped that the staff of the Institute of Ophthalmology will complete the textbook on ophthalmic surgery which he had begun, as a contribution to his memory.

F. PHINIZY CALHOUN, M.D.

Dr. Wheeler's birthplace, Burlington, Vt., is one of the most beautiful of small cities and the site of the state university. His father was much like him, a modest, unassuming man who came home from the Civil War to raise and educate a family on the limited income of a country lawyer. This he supplemented for over thirty years by the nominal salaries of superintendent of public schools and treasurer of the university.

Dr. Wheeler was educated in these schools and afterward received both his academic and his medical degrees at the university. By all present standards it was a very inadequate education, though there was nothing better to be had at the time. The university was a small one, with little endowment and less material equipment, but it had on its faculty a few men who were really great personalities and inspiring teachers. It offered the additional advantage of being almost unbelievably inexpensive.

His boyhood environment was one of the great factors in Dr. Wheeler's life. Here he acquired his salty humor and his eagerly collected fund of Vermont stories. Here he returned to marry his boyhood playmate, who became not only his devoted wife and the mother of his children but the confidant who shared all his hopes and plans. Here he returned year after year for rest and relaxation. Here he built the beautiful log camp in the mountains in which during many summers he kept open house for his friends, and here he returned, unknowingly, to die.

Dr. Wheeler had the temperament of the great surgeon, the willingness to assume responsibility, the ability to rise to emergencies and, when he had done his best, the ability to banish worry.

As the older men retired, his reputation grew, not because he was pushful or aggressive but because of his universally conceded ability.

He loved teaching and the training of assistants and students, and his operative clinics were always crowded. He was a firm disciplinarian,

but for the men who did things just as he wanted them done he spared neither time nor trouble in the training, while his interest and assistance followed them long after they had become established in other fields.

He had the unique ability of inspiring subordinates and building up an esprit de corps among them, of assigning to each the tasks appropriate to his ability; of encouraging them to do original work, often work he had hoped some time to do himself. He naturally could select his subordinates from the whole country, for to have been trained by Dr. Wheeler was almost a guarantee of success in any community.

No man ever more enjoyed the affection of his associates and his subordinates. No man ever inspired less jealousy and ill will.

He was, of course, a great surgeon, for he not only did superlatively the operations that his predecessors had devised but originated many new operations or made improvements on the old. In the World War he was assigned the care of the mass of unfortunates who returned to this country crippled or disfigured by wounds and hasty operations. He developed out of this supposedly hopeless task a marvelous technic of plastic surgery, which seems likely to put him among the ophthalmologic immortals.

As he grew older and his reputation increased, more and more of the desperate cases were referred to him for a final judgment, when the chances of failure even at his hands were often far greater than the chances of success.

He was an ideal consultant, always helpful and understanding and willing to assume responsibility. He often went far beyond the bare requirements of medical ethics in his efforts to avoid criticism or to save the face of a colleague. His thoughtfulness and kindness for his patients whether rich or poor were proverbial.

He was for many years an active supporter of the National Society for the Prevention of Blindness, and in 1931 became one of the organization's directors and one of the most useful members of its board.

In 1936 he was awarded the Leslie Dana Medal, bestowed each year on some layman or physician for conspicuous service in the prevention of blindness, his medal being fittingly inscribed, "Skilled surgeon, great teacher, understanding and sympathetic physician and friend."

Notwithstanding the catastrophe which befell him a few years ago, with steadfast courage he convinced himself and his associates that he could still operate up to his own high standards and kept up his work, both executive and surgical, to the very end. His last years were in many respects his greatest ones.

ELLICE M. ALGER, M.D.

Book Reviews

An Introduction to the Mathematics of Ophthalmic Optics. By Paul Boeder, Ph.D. Price, $2.50. Pp. 244, including index. Rutland, Vt.: Tuttle Company, Inc., 1937.

This little book is so easy to read that it must have been quite difficult to write.

Its greatest asset is the extreme simplicity and lucidity with which the subject matter is presented. Even the reader who has forgotten all of his high school mathematics may nevertheless rely on Boeder to carry him through to an elementary understanding of the theory of Gauss.

The introduction consists of a brief discussion of measurement and numbers. This is followed in part I by a brief review of the arithmetic of fractions and a discussion of negative numbers.

Part II deals with elementary algebra. The diopter is defined. Expressions for the dioptric power of a surface and that of a thick lens are introduced. The author's discussion of the information to be derived from manipulation of the formula

$$D_e = \frac{D_1}{1-dD_1} + D_2$$

is particularly effective in demonstrating the power of the mathematical attack.

The derivation of the formulas for the conjugate distances and magnification of a two surface system is clear and explicit. The formulas are developed with the vertices, focal points and principal points as reference points. The optical system formed by the combination of a reduced eye and a correcting lens is discussed.

Part III treats of geometry and trigonometry. Among other topics discussed are the geometric method of image construction, the lens gage, the entrance and exit pupils of the eye, Snell's laws and reflection by plane and spherical mirrors.

There is a compact index to formulas in addition to the usual index.

The illustrations are numerous, simple and effective. Almost all the examples and applications deal specifically with ophthalmic optics. Answers to the examples are supplied.

The book is admirably suited to the needs of the unaided reader. An adverse criticism which might be made is that after the discussion of the algebraic method in part II, the geometry and trigonometry of part III, although adequately treated, seem somewhat of a regression. When the author has gone so far, one wishes that he would go further. A development of the matrix evaluation of the Gauss coefficients for a three surface system might be substituted for part III. This would considerably enlarge the scope of the book, permitting, for example, the introduction of the schematic eye and a discussion of telescopic spectacles. Boeder's unusual expository ability should make even these relatively difficult subjects clear and thus bring the book to a fitting climax.

ELEK LUDVIGH.

Neuro-Ophthalmology. By R. Lindsay Rea, London. Price, $9. Pp. 568, with illustrations. St. Louis: C. V. Mosby Company, 1938.

This book is dedicated to the memory of the late Prof. Johnson Symington, who occupied the chair of anatomy in Queen's University at Belfast, Ireland.

It is intended for ophthalmologists working in neurologic hospitals and for students in neurology and to facilitate the cooperation of the ophthalmologist and the neurologist in the study of their connecting subjects.

After a short introduction on the functional examination of the eye required in the study of diseases of the nervous system, the anatomy and disturbances of the pupil and the muscles and nerves of the eye are carefully described; then follow descriptions of lesions of the optic nerve, such as papilledema, atrophy of the optic nerve, lesions of visual tracts, with the localizing signs as brought out by the study of the visual fields, and lesions of the macula. The localizing value of ocular symptoms in diseases of the brain forms an important chapter. Congenital and degenerative abnormalities, subarachnoid hemorrhage, tumors of the optic nerve, the region of the optic chiasm and pituitary body, ocular manifestations in diseases of the nervous system, diseases of the vegetative nervous system, ocular manifestations of head injuries, poisons which affect vision, headache and amaurosis are the subjects treated in the remaining chapters.

This shows that the author has assembled a vast amount of information which is clearly and logically presented and well illustrated. There are a few points on which some difference of opinion is permissible, but none of them are of sufficient importance to need comment. Dr. Rea is to be commended for the admirable manner in which he has presented a difficult subject. There has been a definite need for such a presentation, as there has been no recent book on the neurology of the eye in English. The many advances which have taken place in neurology have been fully noted, and Rea's "Neuro-Ophthalmology" is up-to-date and will be a welcome addition to the library of every ophthalmologist.

ARNOLD KNAPP.

Eingriffe am Auge. By Prof. L. von Blaskovics and Prof. A. Kreiker. Price, 20.25 marks. Pp. 454, with 648 illustrations. Stuttgart: Ferdinand Enke, 1938.

It is fortunate that a German translation of Blaskovics' textbook is now available. The original work was published in Hungarian about one year ago and was reviewed in the March 1937 issue of the ARCHIVES, page 567. The German edition has been written by Prof. A. Kreiker, a former assistant of Professor Blaskovics and now his successor as director of the University Eye Clinic in Debrecen, Hungary. Some additions have been made, and the important subject of the operative treatment of detachment of the retina has been enlarged and rewritten. Blaskovics' outstanding contribution to ophthalmology has been the surgical correction of lesions and deformities of the eyelids. It is natural, therefore, that the chapter on the eyelids takes up about one half

of the volume and contains a description of many of the operations which have made the author famous. Blaskovics has been a pioneer in developing new methods in this field and from the first established himself as a master in plastic surgery.

The study of these operative procedures will be of the greatest interest and value to every ophthalmologist who does surgical work. An outstanding feature of the book is the excellent illustrations, and their value, particularly in describing the different steps in an operation, cannot be exaggerated. The book making, both for clarity of text and illustrations, deserves praise, and the price is most reasonable.

ARNOLD KNAPP.

Fundus oculi. Diagnostica oftalmoscopica. By Prof. Q. Di Marzio, Bologna. L. Salomone, Rome: 1937.

The guiding principle of this atlas, dedicated to Benito Mussolini, is to demonstrate the usefulness of the ophthalmoscope in general diagnosis. It contains 100 large plates with 212 drawings which have been reproduced from original oil paintings by the modern method of offset calcolithography. The pictures are reproduced in the upright image as seen by the ophthalmoscope of Gullstrand. The courses of many of the conditions are presented, so that a comprehensive picture is given. A brief description of the fundus lesion and a brief history, including the results of roentgen examination and examination of the visual fields, which explain the relation to general disease, accompany each drawing.

The subject matter is arranged in the following order: normal eyegrounds, congenital anomalies and diseases of the optic nerve, of the retina and of the choroid. Among the illustrations, those which are outstanding and unusual are those depicting tumor at the head of the optic nerve, serous meningitis, cystic opticochiasmic arachnoiditis, hemorrhagic retinitis in chronic myeloid leukemia, tuberculous retinal periphlebitis, preretinal cysticercus, many examples of detachments with holes before and after operation and traumatic peripapillary rupture of the hyaloid membrane.

The author is to be complimented on the publication of a most instructive atlas. The reproductions in colors are lifelike and excellent. reflecting great credit on the artist and on the publishers.

ARNOLD KNAPP.

Les médications de choc en ophthalmologie. By L. Hambresin. Pp. 252, with 11 illustrations. Paris: Masson & Cie, 1937.

This volume is the tenth annual monograph of the French Ophthalmological Society.

By the expression *choc thérapeutique,* the French mean any induced upset in physiologic equilibrium which begins and ends abruptly, leaving behind it no lasting anatomic lesion. English-speaking ophthalmologists are prone to speak of the agent used—protein therapy, hemotherapy, etc.—ignoring the manner in which the upset is produced. When this slight difference in conception is understood, the scope and value of this monograph become apparent.

The symptoms of therapeutic shock depend on the agent employed, the dose and the site and method of employment. In most cases injection of the foreign substance is followed by a chill, arterial hypotension and slow pulse. Later the temperature rises sharply, the pulse becomes more rapid and the blood pressure increases. All degrees of these basic phenomena may be encountered.

In most patients therapeutic shock may be induced with safety; but the method should not be used in the presence of tuberculosis, diabetes or cardiac disease. Great care should be exercised in applying the treatment to those persons in whom the presence of asthma or urticaria indicates an allergic diathesis.

The agents injected to produce therapeutic shock are the peptones, milk, charcoal, the various therapeutic serums and vaccines (both specific and nonspecific) and the colloidal forms of gold, silver and sulfur. Turpentine is used to form a local abscess. Whole blood may be used (autohemotherapy) or serum only (autoserotherapy). In all cases the effect is heightened by the appearance of fever, which may also be produced by the induction of malaria and by the Kettering hypertherm.

Many diseases are listed as being benefited by therapeutic shock. To the well known inflammatory lesions commonly accepted as being helped by the procedure, the author adds ocular pemphigus, glaucoma, muscular paralysis and ophthalmic migraine.

If one shock-producing agent is ineffective, another may be tried. The method should be used as an adjuvant to the older forms of treatment and not as the sole therapeutic procedure. The author believes that whole boiled milk is the agent that will be preferred by most ophthalmologists.

G. M. BRUCE.

Les méningiomes supra-sellaires. Diagnostic du syndrome chiasmatique. By Dr. Louis Guillaumat, Paris. Price, 30 francs. Pp. 205. Paris: Gaston Doin & Cie, 1938.

This monograph begins with a description of the normal anatomy of the suprasellar region; the clinical symptoms and roentgen findings in cases of suprasellar meningioma, based on 22 cases observed in the neurosurgical service of Clovis Vincent in the Hôpital de la Pitié, are then fully described. Certain clinical groups are identified, and their diagnosis and treatment are carefully considered. Suprasellar meningiomas arise from the tuberculum sellae and from the jugum sphenoidale. Those arising from the tuberculum sellae are small and must be carefully dissected between the clinoid processes and the optic nerves; those arising from the jugum sphenoidale are larger and may grow to occupy the interhemispheric space, raising and separating the frontal lobes. The former raise the chiasm and cause bitemporal hemianopia. The tumors which arise more anteriorly have time to reach a certain size before making any contact with the optic nerves, and the unilateral preponderance of their development is shown by nonsymmetric changes in the visual field, loss of vision on one side with a temporal defect on the other or a central scotoma caused by intracranial compression on an optic nerve. A transitional form resembles a tumor of the olfactory groove and a tumor arising from the lesser sphenoid wing. In the

growth of the tumor, functional disturbances are produced from compression of the third ventricle and of the frontal lobes. The most noticeable symptom of pressure on the neighboring organs is involvement of the optic nerves and secondly of the optic chiasm. The ocular symptoms consist in atrophy of the optic nerve with occasional slight edema which clouds the margin of the disk. This atrophy may be bilateral, as in 13 cases in the series of 22, or unilateral, as in 6 cases, in 3 of which the Foster Kennedy syndrome was present. Bilateral papilledema was present in 2 cases, and the fundus was normal in 1. As for the defects in the visual field, typical bitemporal defects are not the rule, and the lesions are irregular. Of 19 cases, the defect was bitemporal in 16, homonymous in 1, horizontal in 1 and concentric with scotoma in 1. The signs of intracranial hypertension, the participation of neighboring structures and the roentgen findings are considered in turn.

The diagnosis of supprasellar meningioma usually rests on the defect of the visual field, the roentgenographic picture and the course of the disease. An excellent chapter is devoted to differential diagnosis. The diagnosis of suprasellar meningioma is often difficult. Thus, in these 22 cases the clinical diagnosis was made only in 10. In 6 an adenoma was suspected; in 2, opticochiasmic arachnoiditis, in 3, a meningioma of the lesser wing of the sphenoid bone, and in 1, meningioma of the right frontal area.

As to the prognosis in the 22 cases, 8 of the patients died after the operation, 3 could not be followed, 1 recovered some sight and the vision of the rest was improved. The only treatment is operation. The case histories are fully reported.

In conclusion, the author states that the study of suprasellar meningiomas is only a chapter in the etiology of chiasmic compression; it suggests the important role that the vessels of the circle of Willis play in causing hemianopias and the necessity of considering the surgical treatment of certain types of atrophy of the optic nerve.

Dr. Guillaumat has written a most scholarly and instructive treatise, which can be recommended for careful study by the ophthalmologist and the neurologist.

ARNOLD KNAPP.

CORRECTION

A typographic error occurred in the review of "A Child's Graded Reading Book for Eye Specialists" by Dr. Henry R. Nesburn and Mr. Daniel L. Risley, in the October issue (ARCH. OPHTH. **20**:697, 1938). The price was published as $15.00 instead of $1.50.

Directory of Ophthalmologic Societies *

INTERNATIONAL

International Association for Prevention of Blindness

President: Dr. P. Bailliart, 66 Boulevard Saint-Michel, Paris, 6e, France.
Secretary-General: Prof. M. Van Duyse, Université de Gand, Gand, Prov. Ostflandern, Belgium.
All correspondence should be addressed to the Secretariat, 66 Boulevard Saint-Michel, Paris, 6e, France.

International Ophthalmologic Congress

Secretary: Dr. E. Marx, Costzeedijk 316, Rotterdam, Netherlands.

International Organization Against Trachoma

President: Dr. A. F. MacCallan, 33 Welbeck St., London, W., England.

FOREIGN

British Medical Association, Section on Ophthalmology

President: Dr. Stewart Duke-Elder, 59 Harley St., London, W. 1.
Secretary: Dr. Thomasina Belt, 13 Mitchell Ave., Jesmond, Newcastle-on-Tyne.

Chinese Ophthalmology Society

President: Dr. C. H. Chou, 363 Avenue Haig, Shanghai.
Secretary: Dr. F. S. Tsang, 221 Foochow Rd., Shanghai.

Chinese Ophthalmological Society of Peiping

President: Dr. H. T. Pi, Peiping Union Medical College, Peiping.
Secretary: Dr. C. K. Lin, 180 Hsi-Lo-yen, Chienmeng, Peiping.
Place: Peiping Union Medical College, Peiping. Time: Last Friday of each month.

German Ophthalmological Society

President: Prof. W. Lohlein, Berlin.
Secretary: Prof. E. Engelking, Heidelberg.

Midland Ophthalmological Society

President: Dr. W. Niccol, 4 College Green, Gloucester, England.
Secretary: T. Harrison Butler, 81 Edmund St., Birmingham, England.
Place: Birmingham and Midland Eye Hospital.

Ophthalmological Society of Egypt

President: Prof. Dr. Mohammed Mahfouz Bey, Government Hospital, Alexandria.
Secretary: Dr. Mohammed Khalil, 4 Baehler St., Cairo.
All correspondence should be addressed to the Secretary, Dr. Mohammed Khalil.

Ophthalmological Society of the United Kingdom

President: Mr. T. Harrison Butler, 61 Newhall St., Birmingham, 3.
Secretary: Mr. L. H. Savin, 7 Queen St., Mayfair, W. 1.

Ophthalmology Society of Bombay

President: Dr. D. D. Sathaye, 127 Girgaum Road, Bombay 4, India.
Secretary: Dr. H. D. Dastur, Dadar, Bombay 14, India.
Place: H. B. A. Free Ophthalmic Hospital, Parel, Bombay 12. Time: First Friday of every month.

* Secretaries of societies are requested to furnish the information necessary to make this list complete and to keep it up to date.

Oxford Ophthalmological Congress

Master: Dr. Percival J. Hay, 350 Glossup Rd., Sheffield 10, England.
Hon. Secretary-Treasurer: Dr. F. A. Anderson, 12 St. John's Hill, Shrewsbury, England.
Time: July 1939.

Palestine Ophthalmological Society

President: Dr. Arieh Feigenbaum, Abyssinian Str. 15, Jerusalem.
Secretary: Dr. E. Sinai, Tel-Aviv.

Polish Ophthalmological Society

President: Dr. W. Kapuściński, 2 Waly Batorego, Poznań.
Secretary: Dr. J. Sobański, Lindley'a 4, Warsaw.
Place: Lindley'a 4, Warsaw.

Royal Society of Medicine, Section of Ophthalmology

President: Dr. Malcolm Hepburn, 111 Harley St., London, W. 1, England.
Secretary: Dr. C. Dee Shapland, 15 Devonshire Pl., London, W. 1, England.

Société Française d'Ophtalmologie

Secretary: Dr. René Onfray, 6 Avenue de la Motte Picquet, Paris, 7e.

Society of Swedish Ophthalmologists

President: Prof. K. G. Ploman, Stockholm.
Secretary: Dr. K. O. Granström, Södermalmstorg 4 III tr., Stockholm, Sö.

Tel-Aviv Ophthalmological Society

President: Dr. D. Arieh-Friedman, 96 Allenby Str., Tel-Aviv, Palestine.
Secretary: Dr. Sadger Max, 9 Bialik Str., Tel-Aviv, Palestine.

Tsinan Ophthalmological Society

Chairman: Dr. Eugene Chan, Cheeloo University School of Medicine, Tsinan, Shantung, China.
Place: Cheeloo University School of Medicine. Time: Last Thursday of alternate months.

NATIONAL

American Medical Association, Scientific Assembly, Section on Ophthalmology

Chairman: Dr. S. Judd Beach, 704 Congress St., Portland, Maine.
Secretary: Dr. Derrick T. Vail Jr., 441 Vine St., Cincinnati.
Place: St. Louis. Time: May 15-19, 1939.

American Academy of Ophthalmology and Otolaryngology, Section on Ophthalmology

President: Dr. Harry S. Gradle, 58 E. Washington St., Chicago.
Executive Secretary-Treasurer: Dr. William P. Wherry, 1500 Medical Arts Bldg., Omaha.

American Ophthalmological Society

President: Dr. Frederick Tooke, 1482 Mountain St., Montreal, Canada.
Secretary-Treasurer: Dr. Eugene M. Blake, 303 Whitney Ave., New Haven, Conn.
Place: Hot Springs, Va.

Canadian Ophthalmological Society

President: Dr. S. Hanford McKee, 1528 Crescent St., Montreal.
Secretary-Treasurer: Dr. J. A. MacMillan, 1410 Stanley St., Montreal.
Place: Montreal. Time: June 19-23, 1939.

NATIONAL SOCIETY FOR THE PREVENTION OF BLINDNESS

President: Mr. William Fellowes Morgan, 50 W. 50th St., New York.
Secretary: Miss Regina E. Schneider, 50 W. 50th St., New York.

SECTIONAL

CENTRAL WISCONSIN SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. L. C. Gardner, 11 N. Main St., Fond du Lac.
Secretary: Dr. G. L. McCormick, 626 S. Central Ave., Marshfield.
Place: Rochester, Minn. Time: Nov. 11, 1938.

NEW ENGLAND OPHTHALMOLOGICAL SOCIETY

President: Dr. Edwin B. Goodall, 101 Bay State Rd., Boston.
Secretary-Treasurer: Dr. Trygve Gundersen, 243 Charles St., Boston.
Place: Massachusetts Eye and Ear Infirmary, 243 Charles St., Boston. Time: 8 p. m., third Tuesday of each month from November to April, inclusive.

PACIFIC COAST OTO-OPHTHALMOLOGICAL SOCIETY

President: Dr. F. C. Cordes, 384 Post St., San Francisco.
Secretary-Treasurer: Dr. C. Allen Dickey, 450 Sutter St., San Francisco.
Place: San Francisco. Time: June 19-22, 1939.

PUGET SOUND ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. H. L. Goss, Cobb Bldg., Seattle.
Secretary-Treasurer: Dr. Purman Dorman, 1115 Terry Ave., Seattle.
Place: Seattle or Tacoma, Wash. Time: Third Tuesday of each month, except June, July and August.

ROCK RIVER VALLEY EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. L. J. Friend, 425 E. Grand Ave., Beloit, Wis.
Secretary-Treasurer: Dr. Thorsten E. Blomberg, 501–7th St., Rockford, Ill.
Place: Rockford, Ill., or Janesville or Beloit, Wis. Time: Third Tuesday of each month from October to April, inclusive.

SAGINAW VALLEY ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. Don M. Howell, Alma, Mich.
Secretary-Treasurer: Dr. Louis D. Gomon, 308 Eddy Bldg., Saginaw, Mich.
Place: Saginaw or Bay City, Mich. Time: Second Tuesday of each month, except July and August.

SIOUX VALLEY EYE AND EAR ACADEMY

President: Dr. R. A. Kelly, 304 N. Main St., Mitchell, S. D.
Secretary-Treasurer: Dr. J. C. Decker, 515 Frances Bldg., Sioux City, Iowa.

SOUTHERN MEDICAL ASSOCIATION, SECTION ON EYE, EAR, NOSE AND THROAT

Chairman: Dr. Grady E. Clay, Medical Arts Bldg., Atlanta, Ga.
Secretary: Dr. John R. Hume, 921 Canal St., New Orleans.

SOUTHWESTERN MICHIGAN TRIOLOGICAL SOCIETY

President: Dr. Carl Wencke, Battle Creek.
Secretary-Treasurer: Dr. A. K. Zinn, Battle Creek.
Time: Third Thursday of alternate months.

WESTERN PENNSYLVANIA EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. C. M. Harris, Johnstown.
Secretary-Treasurer: Dr. C. Wearne Beals, 41 N. Brady St., DuBois.

STATE

Colorado Ophthalmological Society

President: A presiding officer is selected for each meeting alternately until all members have served.
Secretary: Dr. John C. Long, 324 Metropolitan Bldg., Denver.
Place: Capitol Life Bldg., Denver. Time: 7:30 p. m., third Saturday of each month, October to May, inclusive.

Connecticut State Medical Society, Section on Eye, Ear, Nose and Throat

President: Dr. William M. Good, 63 Center St., Waterbury.
Secretary-Treasurer: Dr. S. J. Silverberg, 201 Park St., New Haven.

Eye, Ear, Nose and Throat Club of Georgia

President: Dr. Grady E. Clay, 384 Peachtree St., N. E., Atlanta.
Secretary-Treasurer: Dr. J. Mason Baird, 511 Medical Arts Bldg., Atlanta.

Indiana Academy of Ophthalmology and Oto-Laryngology

President: Dr. C. W. Rutherford, 23 E. Ohio St., Indianapolis.
Secretary: Dr. Marlow W. Manion, 23 E. Ohio St., Indianapolis.
Place: Indianapolis. Time: First Wednesday in April.

Iowa Academy of Ophthalmology and Oto-Laryngology

President: Dr. H. H. Lamb, American Bank Bldg., Davenport.
Secretary-Treasurer: Dr. B. M. Merkel, 604 Locust St., Des Moines.
Place: Davenport.

Louisiana-Mississippi Ophthalmological and Otolaryngological Society

President: Dr. Francis E. Le Jeune, 632 Maison Blanche Bldg., New Orleans.
Secretary-Treasurer: Dr. Edley H. Jones, 1301 Washington St., Vicksburg, Miss.
Place: Gulfport, Miss. Time: May 8, 1939.

Michigan State Medical Society, Section of Ophthalmology and Otolaryngology

Chairman: Dr. B. Fralick, 201 S. Main St., Ann Arbor.
Secretary: Dr. O. McGillicuddy, 124 W. Allegan St., Lansing.

Minnesota Academy of Ophthalmology and Otolaryngology

President: Dr. Frank N. Knapp, 318 W. Superior St., Duluth.
Secretary-Treasurer: Dr. George E. McGeary, 920 Medical Arts Bldg., Minneapolis.
Time: Second Friday of each month from October to May.

Montana Academy of Oto-Ophthalmology

President: Dr. Roy Grigg, Bozeman.
Secretary: Dr. A. W. Morse, 507 Phoenix Bldg., Butte.

New Jersey State Medical Society, Section on Ophthalmology, Otology and Rhinolaryngology

Chairman: Dr. Norman W. Burritt, 30 Beechwood Rd., Summit.
Secretary: Dr. A. Russell Sherman, 671 Broad St., Newark.
Place: Atlantic City. Time: June 1939.

New York State Medical Society, Eye, Ear, Nose and Throat Section

Chairman: Dr. Algernon B. Reese, 73 E. 71st St., New York.
Secretary: Dr. Chester C. Cott, 333 Linwood Ave., Buffalo.

North Carolina Eye, Ear, Nose and Throat Society

President: Dr. J. M. Lilly, 302 Old St., Fayetteville.
Secretary-Treasurer: Dr. Frank C. Smith, 106 W. 7th St., Charlotte.

North Dakota Academy of Ophthalmology and Oto-Laryngology

President: Dr. N. A. Youngs, 322 De Mers Ave., Grand Forks.
Secretary-Treasurer: Dr. F. L. Wicks, 516-6th St., Valley City.
Place: Fargo. Time: May 1939.

Oregon Academy of Ophthalmology and Oto-Laryngology

President: Dr. L. O. Clement, 406 State St., Salem.
Secretary-Treasurer: Dr. Paul Bailey, 833 S. W. 11th Ave., Portland.
Place: Good Samaritan Hospital, Portland. Time: Third Tuesday of each month.

Rhode Island Ophthalmological and Otological Society

Acting President: Dr. N. Darrell Harvey, 112 Waterman St., Providence.
Secretary-Treasurer: Dr. Linley C. Happ, 124 Waterman St., Providence.
Place: Rhode Island Medical Society Library, Providence. Time: 8:30 p. m., second Thursday in October, December, February and April.

South Carolina Society of Ophthalmology and Otolaryngology

President: Dr. S. B. Fishburne, 1430 Marion St., Columbia.
Secretary: Dr. J. W. Jervey Jr., 101 Church St., Greenville.
Place: Columbia. Time: Nov. 1, 1938.

Tennessee Academy of Ophthalmology and Otolaryngology

President: Dr. Kate Savage Zerfoss, 165–8th Ave., N., Nashville.
Secretary-Treasurer: Dr. W. D. Stinson, 805 Medical Arts Bldg., Memphis.

Texas Ophthalmological and Oto-Laryngological Society

President: Dr. T. E. Fuller, 100 W. Board St., Texarkana.
Secretary: Dr. O. M. Marchman, 1719 Pacific Ave., Dallas.

Utah Ophthalmological Society

President: Dr. V. P. White, 143½ S. Main St., Salt Lake City.
Secretary-Treasurer: Dr. E. B. Fairbanks, Boston Bldg., Salt Lake City.
Time: Third Monday of each month.

Virginia Society of Oto-Laryngology and Ophthalmology

President: Dr. Charles T. St. Clair, 418 Bland St., Bluefield, W. Va.
Secretary-Treasurer: Dr. M. H. Williams, 30½ Franklin Rd., S. W., Roanoke.

West Virginia State Medical Association, Eye, Ear, Nose and Throat Section

President: Dr. George Traugh, 309 Cleveland Ave., Fairmont.
Secretary: Dr. Welch England, 621½ Market St., Parkersburg.

LOCAL

Academy of Medicine of Northern New Jersey, Section on Eye, Ear, Nose and Throat

President: Dr. Andrew Rados, 31 Lincoln Park, Newark.
Secretary: Dr. William F. McKim, 317 Roseville Ave., Newark.
Place: 91 Lincoln Park South, Newark. Time: 8:45 p. m., second Monday of each month, October to May.

Akron Academy of Ophthalmology and Otolaryngology

President: Dr. L. E. Brown, Second National Bldg., Akron, Ohio.
Secretary-Treasurer: Dr. C. R. Anderson, 106 S. Main St., Akron, Ohio.
Time: First Monday in January, March, May and November.

Atlanta Eye, Ear, Nose and Throat Society

President: Dr. J. Mason Baird, Medical Arts Bldg., Atlanta, Ga.
Secretary: Dr. Alton V. Hallum, 478 Peachtree St., Atlanta, Ga.
Place: Academy of Medicine, 38 Prescott St. Time: Second Friday of each month from October to May.

Baltimore Medical Society, Section on Ophthalmology

Chairman: Dr. Frank B. Walsh, Wilmer Institute, Johns Hopkins Hospital, Baltimore.
Secretary: Dr. Fred M. Reese, 6 E. Eager St., Baltimore.
Place: Medical and Chirurgical Faculty, 1211 Cathedral St. Time: 8:30 p. m., fourth Thursday of each month from October to May.

Brooklyn Ophthalmological Society

President: Dr. E. Clifford Place, 59 Livingston St., Brooklyn.
Secretary-Treasurer: Dr. Frank Mallon, 1135 Park Pl., Brooklyn.
Place: Kings County Medical Society Bldg., 1313 Bedford Ave. Time: Third Thursday in February, April, May, October and December.

Buffalo Ophthalmologic Club

President: Dr. Ivan J. Koenig, 40 North St., Buffalo.
Secretary-Treasurer: Dr. Meyer H. Riwchun, 367 Linwood Ave., Buffalo.
Time: Second Thursday of each month.

Chattanooga Society of Ophthalmology and Otolaryngology

President: Each member, in alphabetical order.
Secretary: Dr. A. H. Benz, 706 Medical Arts Bldg., Chattanooga, Tenn.
Place: Mountain City Club. Time: Second Thursday of each month from September to May.

Chicago Ophthalmological Society

President: Dr. Georgiana Dvorak-Theobald, 715 Lake St., Oak Park, Ill.
Secretary-Treasurer: Dr. Earle B. Fowler, 55 E. Washington St., Chicago.
Place: Medinah Michigan Avenue Club, 505 N. Michigan Ave. Time: Third Monday of each month from October to May.

Cincinnati Ophthalmic Club

Chairman: Each member, in rotation.
Secretary-Treasurer: Dr. E. R. Thomas, 819 Carew Tower, Cincinnati.
Place: Holmes Memorial Library, Cincinnati General Hospital. Time: 8:15 p. m., third Monday of each month except June, July and August.

Cleveland Ophthalmological Club

Chairman: Dr. Paul Moore, Republic Bldg., Cleveland.
Secretary: Dr. G. Leslie Miller, 14805 Detroit Ave., Cleveland.
Time: Second Tuesday in October, December, February and April.

College of Physicians, Philadelphia, Section on Ophthalmology

Chairman: Dr. Alexander G. Fewell, 1924 Pine St., Philadelphia.
Clerk: Dr. W. S. Reese, 1901 Walnut St., Philadelphia.
Time: Third Thursday of every month from October to April, inclusive.

Columbus Ophthalmological and Oto-Laryngological Society

Chairman: Dr. Hugh G. Beatty, 150 E. Broad St., Columbus, Ohio.
Secretary-Treasurer: Dr. W. A. Stoutenborough, 21 E. State St., Columbus, Ohio.
Place: Deshler Wallick Hotel. Time: 6 p. m., first Monday of each month.

Corpus Christi Eye, Ear, Nose and Throat Society

Chairman: Dr. Edgar G. Mathis, 416 Chaparral St., Corpus Christi, Texas.
Secretary: Dr. E. King Gill, 416 Chaparral St., Corpus Christi, Texas.
Time: Second Thursday of each month from October to May.

Dallas Academy of Ophthalmology and Oto-Laryngology

President: Dr. Lester H. Quinn, 4105 Live Oak, Dallas, Texas.
Secretary: Dr. J. Dudley Singleton, 1719 Pacific Ave., Dallas, Texas.
Place: Dallas Athletic Club. Time: 6:30 p. m., first Tuesday of each month from October to June. The November, January and March meetings are devoted to clinical work.

Des Moines Academy of Ophthalmology and Otolaryngology

President: Dr. E. G. Linn, 604 Locust St., Des Moines, Iowa.
Secretary-Treasurer: Dr. Grace Doane, 614 Bankers Trust Bldg., Des Moines, Iowa.
Time: 7:45 p. m., third Monday of every month from September to May.

Detroit Ophthalmological Club

Chairman: Members rotate alphabetically.
Secretary: Dr. William Fowler, 1066 Maccabee Bldg., Detroit.
Time: 6:30 p. m., first Wednesday of each month.

Eastern New York Eye, Ear, Nose and Throat Association

President: Dr. L. A. Hulsebosch, 191 Glen St., Glen Falls.
Secretary-Treasurer: Dr. Joseph L. Holohan, 330 State St., Albany.
Time: Third Wednesday in October, November, March, April, May and June.

Fort Worth Eye, Ear, Nose and Throat Society

President: Dr. R. A. Gough, 602 W. 10th St., Fort Worth, Texas.
Secretary-Treasurer: Dr. Charles R. Lees, 806 Medical Arts Bldg., Fort Worth, Texas.
Place: Medical Hall, Medical Arts Bldg. Time: 7:30 p. m., first Friday of each month except July and August.

Grand Rapids Eye, Ear, Nose and Throat Society

President: Dr. Dewey R. Heetderks, 405 Medical Arts Bldg., Grand Rapids, Mich.
Secretary-Treasurer: Dr. Robert G. Laird, 116 E. Fulton St., Grand Rapids, Mich.
Place: Various local hospitals. Time: Third Thursday of alternating months, September to May.

Houston Academy of Medicine, Eye, Ear, Nose and Throat Section

President: Dr. Louis Daily, 1215 Walker Ave., Houston, Texas.
Secretary: Dr. Herbert H. Harris, 1004 Medical Arts Bldg., Houston, Texas.
Place: Medical Arts Bldg., Harris County Medical Society Rooms. Time: 8 p. m., second Thursday of each month from September to June.

INDIANAPOLIS OPHTHALMOLOGICAL AND OTOLARYNGOLOGICAL SOCIETY

President: Dr. J. K. Leasure, 23 E. Ohio St., Indianapolis.
Secretary: Dr. Kenneth L. Craft, 23 E. Ohio St., Indianapolis.
Place: University Club. Time: 6:30 p. m., second Thursday of each month from October to June.

KANSAS CITY SOCIETY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. E. N. Robertson, Concordia, Kan.
Secretary: Dr. John S. Knight, 1103 Grand Ave., Kansas City, Mo.
Time: Third Thursday of each month from October to June. The November, January and March meetings are devoted to clinical work.

LONG BEACH EYE, EAR, NOSE AND THROAT SOCIETY

Chairman: Dr. Ben K. Parks, 619 Professional Bldg., Long Beach, Calif.
Secretary-Treasurer: Dr. Paul Nilsson, 211 Cherry Ave., Long Beach, Calif.
Place: Professional Bldg. Time: Last Wednesday of each month from October to May.

LOS ANGELES SOCIETY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. Clifford B. Walker, 427 W. 5th St., Los Angeles.
Secretary-Treasurer: Dr. John P. Lordan, 2007 Wilshire Blvd., Los Angeles.
Place: Los Angeles County Medical Association Bldg., 1925 Wilshire Blvd. Time: 6:30 p. m., fourth Monday of each month from September to May, inclusive.

LOUISVILLE EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. Gaylord C. Hall, Brown Bldg., Louisville, Ky.
Secretary-Treasurer: Dr. Charles K. Beck, Starks Bldg., Louisville, Ky.
Place: Brown Hotel. Time: 6:30 p. m., second Thursday of each month from September to May, inclusive.

MEDICAL SOCIETY OF THE DISTRICT OF COLUMBIA, SECTION OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

Chairman: Dr. Earle Breeding, 1801 I St., N. W., Washington.
Secretary: Dr. Elmer Shepherd, 1606–20th St., N. W., Washington.
Place: 1718 M St., N. W. Time: 8 p. m., third Friday of each month from October to April, inclusive.

MEMPHIS SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

Chairman: Each member, in alphabetical order.
Secretary: Dr. Sam H. Sonders, Medical Arts Bldg., Memphis, Tenn.
Place: Eye Clinic of Memphis Eye, Ear, Nose and Throat Hospital. Time: 8 p. m., second Tuesday of each month.

MILWAUKEE OTO-OPHTHALMIC SOCIETY

President: Dr. John E. Mulsow, 231 W. Wisconsin Ave., Milwaukee.
Secretary-Treasurer: Dr. John B. Hitz, 411 E. Mason St., Milwaukee.
Place: University Club. Time: 6:30 p. m., second Tuesday of each month.

MINNEAPOLIS OPHTHALMOLOGICAL SOCIETY

Chairman: Each member, in alphabetical order.
Secretary: Dr. M. C. Pfunder, 645 Medical Arts Bldg., Minneapolis.
Place: Hennepin County Medical Society rooms. Time: 6:30 p. m., fourth Monday of each month, October to May, inclusive.

MONTGOMERY COUNTY MEDICAL SOCIETY

Chairman: Dr. P. H. Kilbourne, Fidelity Bldg., Dayton, Ohio.
Secretary-Treasurer: Dr. Maitland D. Place, 981 Reibold Bldg., Dayton, Ohio.
Place: Van Cleve Hotel. Time: 6:30 p. m., monthly, first Tuesday from October to June, inclusive.

Montreal Ophthalmological Society

President: Dr. L. de G. Joubert, 690 Dunlop St., Montreal, Canada.
Secretary: Dr. K. B. Johnston, 1509 Sherbrooke St., W., Montreal, Canada.
Time: Second Thursday of October, December, February and April.

Nashville Academy of Ophthalmology and Otolaryngology

Chairman: Dr. Guy Maness, 119–7th Ave., Nashville, Tenn.
Secretary-Treasurer: Dr. Andrew Hollabaugh, Doctors Bldg., Nashville, Tenn.
Place: St. Thomas Hospital. Time: 8 p. m., third Monday of each month from October to May.

New Orleans Ophthalmological and Otolaryngological Society

President: Dr. R. H. Fisher, Chess and Checker Club, New Orleans.
Secretary-Treasurer: Dr. H. F. Brewster, 837 Gravier St., New Orleans.
Place: Eye, Ear, Nose and Throat Hospital. Time: Third Thursday of each month from October to June.

New York Academy of Medicine, Section of Ophthalmology

Chairman: Dr. James W. White, 15 Park Ave., New York.
Secretary: Dr. Rudolf Aebli, 30 E. 40th St., New York.
Time: 8:30 p. m., third Monday of every month from October to May, inclusive.

New York Society for Clinical Ophthalmology

President: Dr. Percy Fridenberg, 38 W. 59th St., New York.
Secretary: Dr. David Alperin, 889 Park Place, Brooklyn.
Place: Squibb Hall, 745–5th Ave. Time: 8 p. m., first Monday of each month from October to May, inclusive.

Omaha and Council Bluffs Ophthalmological and Oto-Laryngological Society

President: Dr. Philip Romonek, 107 S. 17th St., Omaha.
Secretary-Treasurer: Dr. W. Howard Morrison, 1500 Medical Arts Bldg., Omaha.
Place: Omaha Club, 20th and Douglas Sts., Omaha. Time: 6 p. m., dinner; 7 p. m., program; third Wednesday of each month from October to May.

Ophthalmological Society of the University of Pittsburgh

President: Dr. W. W. Blair, 121 University Pl., Pittsburgh.
Secretary: Dr. George H. Shuman, 351–5th Ave., Pittsburgh.
Time: Second Monday in November, January, March and May.

Passaic-Bergen Ophthalmological Club

President: Dr. R. N. Berke, 430 Union St., Hackensack, N. J.
Secretary-Treasurer: Dr. T. A. Sanfacon, 340 Park Ave., Paterson, N. J.
Place: Paterson Eye and Ear Infirmary. Time: 9 p. m., last Friday of every month, except June, July and August.

Philadelphia County Medical Society, Eye Section

Chairman: Dr. Walter I. Lillie, 255 S. 17th St., Philadelphia.
Secretary: Dr. Edmund B. Spaeth, 1930 Chestnut St., Philadelphia.
Time: First Thursday of each month from October to May.

Pittsburgh Ophthalmological Society

President: Dr. Edward Stieren, Union Trust Bldg., Pittsburgh.
Secretary: Dr. George H. Shuman, 351-5th Ave., Pittsburgh.
Place: Pittsburgh Academy of Medicine Bldg. Time: Fourth Monday of each month, except June, July, August and September.

Richmond Ophthalmological and Oto-Laryngological Society

President: Dr. N. H. Turner, 200 E. Franklin St., Richmond, Va.
Secretary: Dr. Richard W. Vaughan, Medical Arts Bldg., Richmond, Va.
Place: Westmoreland Club. Time: 6 p. m., second Monday of each month from October to May.

Rochester Eye, Ear, Nose and Throat Society

President: Dr. R. E. Elliott, 78 S. Fitzhugh St., Rochester, N. Y.
Secretary-Treasurer: Dr. Raphael Farber, 280 Monroe Ave., Rochester, N. Y.
Place: Rochester Medical Association, 113 Prince St. Time: 8 p. m., third Monday of each month from October to May.

St. Louis Ophthalmic Society

President: Dr. Roy E. Mason, Frisco Bldg., St. Louis.
Secretary: Dr. Leslie Charles Drews, 508 N. Grand Blvd., St. Louis.
Place: Oscar Johnson Institute. Time: Clinical meeting 5:30 p. m., dinner and scientific meeting 6:30 p. m., fourth Friday of each month from October to April, inclusive, except December.

San Antonio Ophthalmolo-Oto-Laryngological Society

President: Dr. Oscar H. Judkins, 414 Navarro St., San Antonio, Texas.
Secretary-Treasurer: Dr. Wilfred E. Muldoon, 414 Navarro St., San Antonio, Texas.
Place: Bexar County Medical Library. Time: 8 p. m., first Tuesday of each month from October to May.

San Francisco County Medical Society, Section on Eye, Ear, Nose and Throat

Chairman: Dr. Russell Fletcher, 490 Post St., San Francisco.
Secretary: Dr. Avery Morley Hicks, 490 Post St., San Francisco.
Place: Society's Bldg., 2180 Washington St., San Francisco. Time: Fourth Tuesday of every month except May, June, July and December.

Shreveport Eye, Ear, Nose and Throat Society

President: Dr. R. R. Kirkpatrick, 6th and Walnut Sts., Texarkana, Ark.
Secretary-Treasurer: Dr. W. L. Atkins, 940 Margaret Pl., Shreveport, La.
Place: Shreveport Charity Hospital. Time: 7:30 p. m., first Monday of every month except July, August and September.

Spokane Academy of Ophthalmology and Oto-Laryngology

President: Dr. P. B. Greene, 422 Riverside Ave., Spokane, Wash.
Secretary: Dr. O. M. Rott, 421 Riverside Ave., Spokane, Wash.
Place: Paulsen Medical and Dental Library. Time: 8 p. m., fourth Tuesday of each month except June, July and August.

Syracuse Eye, Ear, Nose and Throat Society

President: Dr. James F. Cahill, 428 S. Salina St., Syracuse, N. Y.
Secretary-Treasurer: Dr. I. Herbert Katz, 713 E. Genesee St., Syracuse, N. Y.
Place: University Club. Time: First Tuesday of each month except June, July and August.

Toronto Academy of Medicine, Section of Ophthalmology

Chairman: Dr. A. Lloyd Morgan, 170 St. George St., Toronto, Canada.
Secretary: Dr. W. R. F. Luke, 170 St. George St., Toronto, Canada.
Place: Academy of Medicine, 13 Queen's Pk. Time: First Monday of each month, November to April.

Washington, D. C., Ophthalmological Society

President: Dr. G. Victor Simpson, 1710 Rhode Island Ave., N. W., Washington, D. C.
Secretary-Treasurer: Dr. Frank D. Costenbader, 1726 I St., Washington, D. C.
Place: Episcopal Eye, Ear and Throat Hospital. Time: 8 p. m., first Monday in November, January, March and May.